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## The WHO Multicentre Growth Reference Study (MGRS): Rationale, planning, and implementation

*Mercedes de Onis (WHO), Cutberto Garza (UNU), Cesar G. Victora (Brazil),  
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# Preface

*“A future of sustainable development begins with safeguarding the health of every child.”*

*Kofi A. Annan*  
*Secretary-General of the United Nations*

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Among the indisputable rights of children is the right to health. Without respecting this right and providing the necessary resources to secure it, we cannot hope to achieve any of the major development goals the world has united around in the United Nations Millennium Declaration. Human capital is essential to all development. Without basic health and nutrition, the potential of our children goes to waste.

Growth references are among the most valuable and widely used tools we have to measure how we manage to fulfill children's basic physical needs. Of course, assessing growth alone is not enough to adequately evaluate an individual's health status. But his or her physical development is a core element.

The usefulness of growth references, however, stretches far beyond that. Because so many physiological processes must “go right” and so many needs must be met in childhood if growth is to proceed normally, divergences and variations within populations and strata can give useful indications of how supportive the children's surroundings are and even help us track our progress in attaining “health for all.” Data collected throughout populations over time can give us important information about their medium- and long-term social and economic development.

Thus, not surprisingly, United Nations and governmental agencies responsible for promoting, securing, and sustaining children's well-being rely on growth references for a wide range of tasks, such as assessing general health status, promoting equity, formulating health and related policies, planning interventions, and monitoring the effectiveness of their efforts and those of others who share commitments and responsibilities to children.

Under the leadership of the World Health Organization (WHO), the United Nations in 1993 undertook a comprehensive review of the uses and interpretation of anthropometric references. As a result of this review, the World Health Assembly (WHA) endorsed the development of a new set of tools to assess infant and young child growth. The Assembly also stressed the need to move beyond past

approaches designed to describe *how children grow in a particular region and time* to the more desirable goal of describing *how all children should grow* when their needs are met. In setting this more ambitious goal, the WHA moved beyond recommending the construction of a *reference*, i.e., a device for grouping and analyzing data, to the development of a *standard* (or as close to one as possible), i.e., a device that embodies the concept of a norm or target, thus enabling a value judgment.

To accomplish this more ambitious goal, WHO and its principal partner, the United Nations University, undertook the Multicentre Growth Reference Study (MGRS). At its core was the recruitment of children who met rigorous standards of health. These children not only had to be free of debilitating diseases, but also had to come from families that had conformed with health recommendations in areas such as breastfeeding and smoking cessation.

Emboldened by WHA's commitment, this effort went two steps further. It recruited children from all of the world's major regions to underscore that all children, regardless of ethnic background or regional origin, grow similarly when their needs are met. Moreover, it linked growth measurements to the assessment of motor development. The latter component was facilitated by key support from UNICEF.

By replacing the present international reference, which is based on children from a single country, with one based on an international group of children, we are significantly strengthening the hand of those working to extend the right to health to all children. Similarly, by linking physical growth to motor development, we highlight the very important point that although normal physical growth is a necessary enabler of human development, it is not sufficient. Attention also must be focused on the functional capacities that normal growth makes possible, but does not assure. Together, these three new elements—the “prescriptive” approach that moves beyond the development of growth references to the approximation of standards, the inclusion of children from around the world, and links to motor development—provide us with a much

better instrument to use in our efforts to meet the needs of the world's children. But it also significantly raises expectations of what we should achieve.

This supplement documents the planning, methods, and implementation of the MGRS. The challenges of its adaptation in six distinct sites—Brazil, Ghana, India, Norway, Oman, and the United States—and the creative approaches used to meet them are evident in its contents. Covering five areas, the supplement:

- » reviews the rationale for developing a new international set of tools to assess infant and child growth;
- » describes the planning, study design, and methodologies adopted to meet the aims of the MGRS;
- » reviews the protocols developed to obtain and standardize anthropometric measurements and motor milestones;
- » outlines the comprehensive and rigorous data management system designed to assure optimal data quality; and
- » systematically considers the site-specific implementation of this global activity.

The outcomes of the MGRS will be scientifically more robust tools to assess child growth than the ones currently available to the international community. Perhaps equally important, these will also be powerful tools for purposes of child health advocacy.

We firmly believe that having tools that provide approximate standards and that are based on children

from all of the world's major regions sends crucial messages about aspects of human development that bind all children, political commitments that enable the biological/physical development of individuals and their communities, and responsibilities that are imposed by the last century's remarkable achievements in health, food and agricultural sectors, and information technology.

This project has been a model example of cooperation and collaboration within the UN family and with its external bilateral partners and civil society, and we take pleasure in that fact. Special recognition is due to literally thousands of volunteers and their families who gave freely of their time to this international effort, the principal investigators and their staffs at each of the study sites, and the hundreds of scientists who served as reviewers and in other advisory roles. Special recognition is also due to the WHO Department of Nutrition for Health and Development for its leadership and day-to-day coordination of this activity; the UNU Food and Nutrition Program for its constant support, leadership, and commitment; and the multiple donors who provided vital financial support, encouragement, and intellectual resources for this activity.

*LEE Jong-wook*  
*Director-General*  
*World Health Organization*

*Hans van Ginkel*  
*Rector*  
*United Nations University*

# Rationale for developing a new international growth reference

Cutberto Garza and Mercedes de Onis, for the WHO Multicentre Growth Reference Study Group

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## Abstract

*The rationale for developing a new international growth reference derived principally from a Working Group on infant growth established by the World Health Organization (WHO) in 1990. It recommended an approach that described how children should grow rather than describing how children grow; that an international sampling frame be used to highlight the similarity in early childhood growth among diverse ethnic groups; that modern analytical methods be exploited; and that links among anthropometric assessments and functional outcomes be included to the fullest possible extent. Upgrading international growth references to resemble standards more closely will assist in monitoring and attaining a wide variety of international goals related to health and other aspects of social equity. In addition to providing scientifically robust tools, a new reference based on a global sample of children whose health needs are met will provide a useful advocacy tool to health-care providers and others with interests in promoting child health.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth monitoring, growth references, growth standards, human rights

## Introduction

Growth references are among the most commonly used and most valuable tools for assessing the general well-being of individuals, groups of children, and the communities in which they live, and for tracking progress in reaching a range of health and other, broader goals related to social equity. The value of growth references resides in the fact that numerous physiological processes must proceed normally and many needs must be met in fetal life and childhood if growth is to proceed normally. Thus, although assessing growth is insufficient as a means of adequately evaluating the health status of an individual or a population, normal physical development is a necessary aim of any strategy that includes aspects of well-being as key outcomes. The marked vulnerability of the health of infants and young children also makes assessments of child growth a “sentinel” indicator in evaluations of the health and socioeconomic development of communities in which they live.

## The 1993 WHO Expert Committee on the use and interpretation of anthropometry

Given the importance of normal growth as a summary indicator for health, it is clearly within the set of responsibilities of the World Health Organization (WHO) to establish norms for it. In keeping with this normative function, the WHO has periodically convened Working Groups and Expert Committees to examine issues related to anthropometry. The most recent WHO Expert Committee to review this topic was convened in 1993 [1].

In the past, WHO’s attention to this topic focused principally on the anthropometry of infants and young children [2–4]. The 1993 Expert Committee, however, was asked to address the use and interpretation of anthropometry throughout the life cycle. This broadened interest signaled an increased appreciation of the utility of anthropometric measurements and indicators

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for the screening and evaluation of the health status of individuals and populations of all ages, and the value of changes in anthropometric measurements in the assessment of progress in meeting health, equity, and other societal goals.

WHO organized seven Working Groups in preparation for the 1993 expert consultation to review issues specifically relevant to pregnant and lactating women, the fetus and newborn infant, infants and young children through 2 years of age, children 2 to 10 years of age, adolescents, adults, and the elderly. The Multicentre Growth Reference Study (MGRS) was a direct result of the deliberations of the Working Group on Infant Growth [5].

### The WHO Working Group on Infant Growth

The Working Group on Infant Growth was charged with developing recommendations for the appropriate uses and interpretation of anthropometry in infants and young children, i.e., for individuals and populations in diverse operational settings; identifying and/or developing reference data for anthropometric indicators; providing guidelines on their uses; and identifying crucial issues and gaps in knowledge in need of further development. From the beginning of its deliberations, the Working Group focused on incongruities presented by the apparent poor growth of healthy breastfed infants of well-nourished women living in favorable environments. This apparent poor growth was inconsistent with the multiple health benefits associated with breastfeeding and other health behaviors associated with these demographic groups and the environments in which they resided. These inconsistencies focused the Working Group's attention on an evaluation of the current international reference, the US National Center for Health Statistics (NCHS)/WHO International Growth Reference [6], and on a systematic review of the growth performance of breastfed infants studied under relatively highly controlled conditions.

### Brief history of the current international reference

The history of the current international growth reference was reviewed in 1996 by de Onis and Yip [7]. This reference was based on a framework initially recommended by the Food and Nutrition Board of the United States National Academy of Sciences [8, 9] and implemented by a joint NCHS and Centers for Disease Control task force [6, 10]. The task force compiled longitudinal data (0 to 23 months) collected by the Ohio Fels Research Institute from various groups of children studied before 1975 and cross-sectional data collected by the US Health Examination Surveys conducted from

1960 to 1975 in children 2 to 18 years of age. The Fels data were collected from predominantly formula-fed infants who resided in a restricted geographic area and were of relatively high socioeconomic backgrounds. The US Health Examination Surveys were designed to reflect representative samples of US children.

During the same period, WHO convened an expert group in 1975 to advise it on the use of anthropometric indicators in nutrition surveys and surveillance activities [11]. This group recommended the use of reference data for these purposes and outlined specific criteria that such data should meet. Although none of the growth data available at that time met the recommended criteria, the NCHS data were recommended by this group for use as the international reference [12]. The major limitations of the infant portion of these data and the reference constructed from them were that the sample was limited to infants of European descent residing in the United States, measurements were taken only every three months, and the analytical methods available at the time were inadequate for the task and were likely to inappropriately depict the pattern and variability of normal growth [7]. The latter two shortcomings contributed to a mischaracterization of the shape of the growth curve, particularly during the first six months when rapid growth occurs, and whose accurate characterization is crucial for effective lactation management.

### Summary of the analyses of the Working Group

To review the growth performance of healthy breastfed infants, the Working Group assembled published and unpublished growth data from infants who were exclusively or predominantly breastfed to at least 4 months and who continued breastfeeding for the first 12 months. The Working Group applied fairly conservative criteria to data selection to maximize the likelihood that the growth pattern of the selected sample was not constrained by environmental factors, the nutritional status of the mother, the index pregnancy, or inadequate lactation support. A sample of 226 infants (109 boys and 117 girls) who met the feeding and other criteria outlined above was selected from the larger set of published and unpublished data available to the Working Group. Although this sample had a broader geographic base than the Fels sample, the "pooled breastfed data set" was also from children predominantly of European background and of relatively high socioeconomic status. Additional details of these analyses have been published elsewhere [5, 13].

Among the more salient findings from these analyses are three results particularly relevant to this discussion. First, it was clear that the growth of this conservatively

selected sample of infants deviated negatively from the current international reference and that the magnitude of the deviation was sufficiently large to interfere with nutritional management. The mean Z scores for length-for-age, weight-for-age, and weight-for-length of children 1 to 12 months of age, calculated on the basis of the current international reference, are summarized in figure 1. Rather than the anticipated approximate tracking of early growth trajectories, weight-for-age Z scores fell progressively from months 2 through 12, Z scores for weight-for-length showed a similar pattern, and those for length-for-age fell through 8 months.

To further evaluate the patterns of growth represented by the current international reference and the pooled breastfed data set, the Working Group examined a data set from a WHO Human Reproduction Programme (HRP) study conducted in five countries: Chile, Egypt, Hungary, Kenya, and Thailand [14]. The HRP data set included 1,273 infants whose geographic origins and socioeconomic status were more diverse than those of infants who comprised either the current international reference or the pooled breastfed data set. The Working Group compared the growth of a subset ( $n = 382$ ) of those infants—those who were either exclusively or predominantly breastfed for various lengths of time through the first year—with both the current international reference and the Working Group's pooled breastfed data set.

The results of the weight-for-age comparison are summarized in figure 2. The Z scores of healthy HRP infants fell from approximately month 3 to months 11 or 12 when the basis for comparison was the current international growth reference, or were sustained or slightly increased when the pooled breastfed data set was used as the reference. The HRP group's declining Z scores relative to the current international reference and its sustained tracking of early Z scores relative to the pooled breastfed data set supported the view that the present international reference was inappropriate for assessing the growth of healthy infants, at least through 12 months of age, and that the growth pattern followed by the pooled breastfed data probably

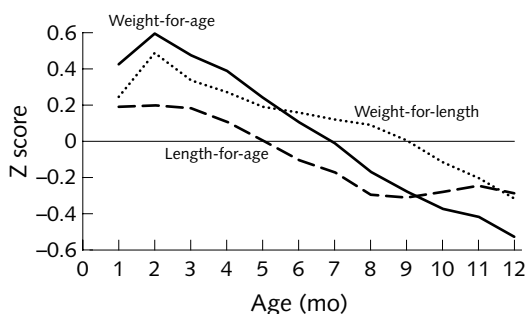


FIG. 1. Mean Z scores of infants in the “pooled breastfed data set” relative to the NCHS/WHO international reference [5]

reflected “physiological growth” more closely than did the current international reference.

The third finding was that the variability of growth in the pooled breastfed data set appeared to be significantly smaller than that of the present international reference. These differences were sustained throughout the first 12 months for length and weight in both males and females. The consequences of the decreased variability are illustrated in figure 3. As is evident from this figure, narrowing the distance between the means and the commonly used statistical cutoffs ( $\pm 2$  SD) to identify children at significant risk for either inadequate or excessive growth significantly influences the classification of individual children into either category and estimates of the prevalence of either condition. The narrower variation in the pooled breastfed data set may have resulted from its conservative selection criteria. Alternatively, the wider variation depicted by the current international growth reference may reflect the apparently broad definition of health used to select the Fels population, i.e., the absence of observable illness and the lack of feeding criteria in selecting the study sample. Artificial milks used at the time the Fels data were collected are no longer available, as manufacturers have improved infant formulas steadily. Thus, wider growth variability may have resulted from responses to “nonoptimal” formulas that subsequently were replaced by others that presumably were improved based upon new knowledge of nutritional needs during infancy.

## Conclusions of the Working Group

The Working Group's interpretation of these and other related findings outlined in its report to WHO [5] led it to conclude that new references were necessary and that it was time to consider the production of references that would more closely approximate standards, i.e., to describe how children *should* grow in all settings rather than to limit oneself to a description of *how* children grow in a specific setting and time.

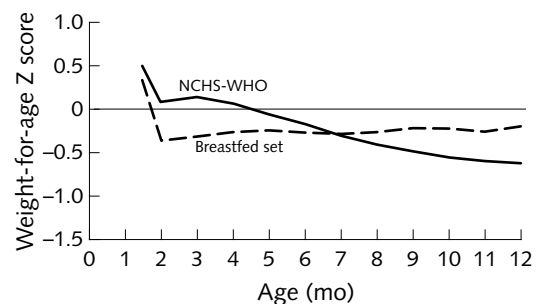


FIG. 2. Mean weight-for-age Z scores of infants enrolled in the WHO Human Reproduction Programme study compared with the NCHS/WHO international reference and the “pooled breastfed data set” [5]

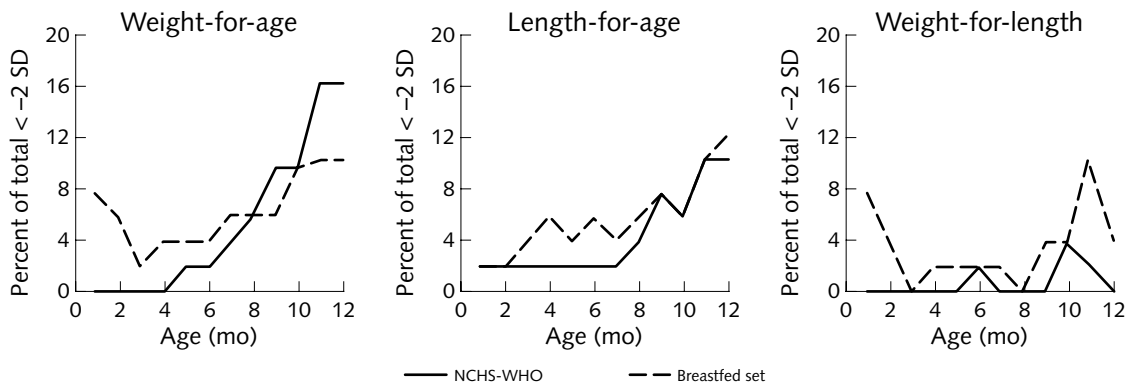


FIG. 3a. Percentages of peri-urban Peruvian infants with weight-for-age, length-for-age, or weight-for-length below the  $-2$  Z score cutoff, according to the NCHS/WHO international reference and the "pooled breastfed data set" [5]

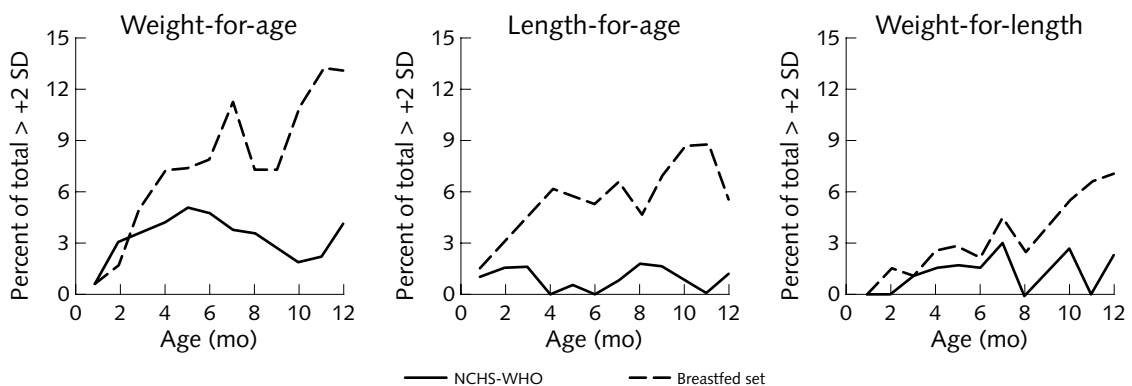


FIG. 3b. Percentages of US and European formula-fed infants with weight-for-age, length-for-age, or weight-for-length above the  $+2$  Z score cutoff, according to the NCHS/WHO international reference and the "pooled breastfed data set" [5]

Three principal lines of thought led to this conclusion. First, the group surmised that at least one key biological assumption inherent in the present international reference is flawed, namely, that infant growth is probably not independent of feeding choices (at least not under conditions that characterized infant feeding choices when the present international reference data were collected). Knowledge of the nutritional, immunological, and reproductive benefits of breastfeeding argues strongly for the breastfed infant as the standard for physiologic growth. The narrower variability estimates derived from the pooled breastfed data set may reflect these biological advantages. The narrow ethnic representation of the pooled breastfed data set is an unsatisfactory explanation for the decreased variability, because of the similarities between the Fels data and the breastfed pooled data set in this regard.

Second, the group recommended that early growth patterns be documented in increments shorter than three months. One possible partial explanation for the deviations between the current international reference and the growth pattern of breastfed infants is that measurements at three-monthly intervals are inadequate to capture the dynamic pattern of growth

in the first six months. An accurate depiction of those patterns was viewed as especially important because of the role that growth monitoring plays in lactation management during this period.

Third, the Working Group concluded that limitations inherent to curve-fitting or smoothing techniques available at the time of construction of the present international reference may be an additional explanation for the observed growth discrepancies. Advances in analytical capabilities and approaches have made methods applied to construct the present international reference outmoded.

In response to these findings and recommendations, WHO convened a group in 1995 to develop a protocol for the development of new growth references. Because of the nature of public health programs, WHO asked this second Working Group to consider the inclusion of children through the age of five years.

### Ancillary analyses

The deliberations of this second Working Group led to additional analyses that were key to the subsequent



design of the MGRS protocol. The rationale for basing a new reference on breastfed infants was clear and reaffirmed by this group; however, the possibility that other health-related behaviors significantly influenced physiologic growth responses was raised in its discussions. Among the issues of most concern were the timing and nature of complementary feeding, the role of nutrient supplements, and selected parental behaviors, most notably smoking and the use of alcohol and other drugs, and the potential for different growth patterns among breastfed infants of diverse ethnicity. Data from a second HRP data set were used [15, 16] to assess each of these issues.

The results of some of these analyses were published subsequent to their availability for planning the MGRS. Growth patterns of breastfed infants from seven countries (Australia, Chile, China, Guatemala, India, Nigeria, and Sweden) were published in 2000 [17]. Multilevel modeling was used to assess between-site growth differences after adjustments for maternal stature and infant feeding pattern. Approximately 120 infants per site were used for these analyses. Although the study was not restricted to socioeconomically advantaged groups, all women who participated were literate and had educational levels well above the average of their countries of residence. Growth patterns were strikingly similar in all countries except China and India. Maternal education was related to infant growth only in India. All sites were urban except for China. Compared with the arbitrarily selected reference group (Australia), Chinese infants were approximately 3% shorter and Indian infants were approximately 15% lighter at 12 months of age. These analyses demonstrated that breastfed infants from economically privileged families (relative to national norms) were very similar despite the wide ethnic differences and diverse geographic characteristics in this second HRP data set. The findings also underscore the utility of the surveys that were undertaken as a prerequisite to the selection of participating sites. This feature of the MGRS is discussed elsewhere in this supplement [18].

The HRP study was also used to assess associations among growth patterns and different durations of exclusive breastfeeding and the types and frequency of complementary foods introduced between four and six months [19]. Small, statistically significant differences in growth were noted among breastfed infants to whom complementary foods were introduced at different times during that interval; however, the magnitudes of those differences were sufficiently small to be biologically unimportant. The most extreme differences were equivalent to approximately 10 centiles of the weight and height distributions at six months of age. These results provided no compelling evidence of benefit or risk from the timing of complementary feeding between four and six months nor from the frequency or types of complementary foods used during

this period by these relatively privileged groups with no major economic constraints and with low rates of infectious illnesses.

In a separate unpublished analysis (report available on request), also based on the second HRP study, associations between the maternal use of alcohol and vitamin or mineral supplements and postnatal infant growth were examined. Alcohol use was examined in the HRP data obtained from Australia, Chile, China, and Sweden. In none of those sites was prenatal or postnatal alcohol use related to postnatal length or weight. The effect of maternal vitamin or mineral supplements was evaluated in the HRP data collected in Australia, Chile, and Sweden. Prenatal or postnatal maternal supplement use was also unrelated to postnatal length or weight in any of those sites.

Maternal use of tobacco was evaluated from the published literature. The second Working Group considered that the effects of smoking on fetal growth [20] and on lactation performance and infant growth [21–23] were important enough to justify inclusion of maternal smoking as an eligibility criterion in the MGRS protocol [18].

## Rationale for the MGRS

These analyses, the deliberations of the Working Groups, and extensive peer reviews of the conclusions and recommendations of both Working Groups culminated in the development of a study protocol and operational framework with four salient features: (a) a clearly “prescriptive” approach that included the consideration of infant feeding choices, maternal support for breastfeeding, maternal smoking, and environmental conditions that supported unconstrained physiologic growth; (b) an international sampling frame; (c) heavy reliance on current information technology and its increasing accessibility to document fully the planning and implementation phases of the study, to implement a level of rigor in data management and quality control commensurate with the construction of biological references or standards, and to avoid constraints on the study’s selection of analytical methods for curve construction (following a systematic review of contemporary approaches for the analysis of longitudinal and cross-sectional data); and (d) a proposed link between anthropometric assessments and specific functional outcomes of predictive relevance to the well-being of children. This proposed link led to the subsequent addition of the motor development component of the study, which is also described in this supplement [24].

By adopting a “prescriptive” approach, the protocol’s design went beyond an update of how children in presumably healthy populations grow at a specific time and place. The MGRS was designed to provide data

that describe “how children *should* grow” by including in the selection criteria of the study specific behaviors that are consistent with current health promotion recommendations (e.g., breastfeeding norms, standard pediatric care, and nonsmoking requirements). Thus, the implemented design advanced beyond the construction of a device for grouping and analyzing data (a *reference*) for the purpose of enabling value-free comparisons, to the explicit recognition of the need for *standards* (or as close to them as possible), i.e., devices that enable value judgments by incorporating norms or targets in their construction.

By including an international sampling frame, the design recognizes the solid evidence that all children grow very similarly for the first five years of life when their physiologic needs are met and their environments support healthy development; nearly all interethnic variability is probably a result of environmental assaults [1, 25–27]. The development of a reference composed of children from all major global regions (in contrast to the present international reference, which is based on children from a single country, the United States) is also likely to be more acceptable for international use. Moreover, it will detract from the perceived need by some to develop country-specific growth norms based on multiple, often inappropriate methods that lead to difficulties in cross-country comparisons and are likely to contribute to faulty national policies. Arguably, the current obesity epidemic in the United States would have been detectable earlier if a prescriptive international reference had been available 20 years ago. An added feature of the design’s combined prescriptive and international aspects is the strengthening of advocacy for child health.

Key criteria of reliably robust standards and references are their reproducibility and accessibility to evaluation. Extensive documentation of all stages of development and implementation is indispensable to achieve these characteristics. Among the most important goals of the proposed standards is to remain relevant for as long as possible. This requires that design, implementation, and methodological aspects of sampling strategies, measurements, data management, and analyses be documented as fully as possible. Achieving high standards in the MGRS protocol for each of these features—some of which are reviewed in depth in this supplement [28, 29]—was a key aim. Advances in, and the growing accessibility of, information technology made the task easier to achieve than in the past. The rationale for insisting that these aspects be given scrupulous attention is strengthened by the certainty that knowledge is increasing regarding the functional consequences of early growth patterns and the health behaviors that enable them [30, 31]. Thus, the relevance of MGRS-derived instruments as standards should be amenable to evaluation for the foreseeable future.

Although, as recognized previously, normal growth

is necessary to health, it is not sufficient. Interest in growth assessments stems largely from their value as screening tools that signal nonspecific problems when growth is abnormal, or a relative degree of assurance that key physical and emotional needs are being met when growth proceeds as expected. Thus, although normal growth is a necessary enabler of the full complement of functional capacities associated with health, it alone does not assure their attainment. Other resources and conditions, such as educational and physical stimulation within the home, must be accessible to ensure that broader developmental milestones are achieved. This was the basic rationale for the inclusion of motor development assessments in the MGRS. Their broad predictive value and the relative ease with which key motor milestones could be documented in a wide array of field settings supported their inclusion [24]. Linking them closely to anthropometric standards also is expected to be of significant educational value to parents and health-care providers. From a policy perspective, their inclusion is intended to focus attention on growth and broader functional capacities in childhood that are key to normal development in subsequent life stages.

## Anticipated results

The MGRS is therefore expected to yield scientifically more robust tools for assessing child growth than are available currently, to strengthen the use of these tools for purposes of child health advocacy, and, because of specific design characteristics discussed in this supplement [18], to provide a wider array of references for expanded uses, e.g., much more appropriate tools for the successful management of early lactation and the monitoring of childhood overweight and obesity.

The current international reference is limited to “attained” measures. This limits the interpretation of anthropometric changes and generally restricts the diagnosis of under- or overnutrition to values that cross a preselected cutoff point assumed to reflect a level of risk for restricted or excessive growth, e.g., the 3rd or 97th centiles, respectively. These are generally interpreted to reflect a level of risk that triggers further evaluation, since only 3% of the target population is expected to be above or below either cutoff; however, for reasons reviewed briefly above, the bases of “value” judgments inherent in such evaluations are problematic, given the “nonprescriptive” nature of sampling schemes upon which the current international reference is based.

International references are currently available only for attained weight-for-age, length/height-for-age, and weight-for-length/height. The MGRS protocol was designed to approximate standards for these and several other attained anthropometric measurements: body mass index (BMI)-for-age, mid-upper-arm

circumference (MUAC)-for-age, head circumference-for-age, subscapular skinfold-for-age, and triceps skinfold-for-age. Additionally, velocity references should be available for a number of growth parameters because of the longitudinal component of the MGRS [18]. Velocity references will most likely be valuable in the early assessment of the risk of overweight in infancy and thus contribute to the early management of this increasingly prevalent and worrisome public health problem. Rather than limiting risk designations to after either state has very likely been achieved, velocity references should enable the identification of children at risk of becoming underweight or overweight. This expanded set of tools is expected to enhance the use and interpretation of anthropometric references, as set out in the 1995 Report of the WHO Expert Committee on this topic [1].

The “prescriptive” sampling scheme described above is also expected to provide improved estimates of the variability of normal growth. These improved estimates should make risk assessments more robust at both the individual and the population levels. If the qualitative differences in variability between the present international reference and the pooled breastfed data set summarized in figure 3 are confirmed by the MGRS, estimates of under- and overnutrition will be impacted, but it is difficult to estimate this quantitatively until analyses of MGRS data are complete.

The selection of breastfed infants as the foundation of new standards also contributes significantly to advocacy in support of current international infant feeding policies [32, 33] and will be much more supportive of lactation management protocols than is the current international reference. The lack of congruence between the feeding histories of infants who contributed to the current international reference and international feeding recommendations unnecessarily sent inconsistent, and potentially confusing, messages. Identifying the breastfed infant as the standard aligns policy with health screening evaluations and potentially provides a goal for manufacturers of infant formula to attain and for national and international regulators to consider in approval processes as new formulations are brought to market.

Broadening the definition of “health” beyond the absence of overt disease to include recommended feeding practices and other health behaviors (e.g., criteria related to maternal smoking behaviors) and selecting infants from populations likely to receive recommended pediatric care should enhance expectations that standards of care and recommended family health-care practices will be accessible to all infants and young children. Tethering such behaviors to the most frequently used health screening tool is thus expected to “raise the bar” substantially in terms of international expectations regarding infant and young child care.

## Significance of anticipated results

Upgrading international growth references to tools that more closely resemble standards has substantial significance for other widely accepted international goals. They are expected to make significant contributions to meeting the UN Millennium Development Goals (MDGs) by directly strengthening the framework necessary to achieve them, especially because these new tools are consistent with the human rights approach at the core of the MDGs. The tools will play direct roles at the national, regional, and international levels in monitoring progress toward meeting four of the seven MDGs and, less directly, the remaining three [34]. Although these goals represent a political consensus, and some may question their long-term relevance, the basic aspirations they embody will most likely remain at the core of efforts to narrow social, economic, and health disparities.

Clearly, MDGs such as the eradication of extreme poverty and hunger, achievement of universal primary education, promotion of gender equality and empowerment of women, and reduction in child mortality will each be reflected in improved child well-being. Conversely, improvements in those broad goals will be unattainable unless needs that support normal physical growth are met. Progress in meeting infant and child growth standards will depend significantly on improving maternal health, and so it is likely that these standards also will contribute to the fifth MDG. Similarly, progress in meeting the growth standards will be impossible if we do not succeed in combating HIV/AIDS, malaria, and other diseases, the sixth MDG. Achieving physiologic growth in young children also is linked inextricably to many of the specific aims that comprise the more general MDGs, e.g., ensuring environmental sustainability.

Finally, it is of seminal importance to recognize the basic role that the UN Human Rights Treaty System plays in motivating international aspirations in health and other sectors. The relevance of the MDGs is fully appreciable only within the context of that treaty system. Among the six pillars of the system is the Convention on the Rights of the Child (in force since September 2, 1990).<sup>\*</sup> This convention recognizes duties and obligations to children that cannot be met without attention to normal human development. The use of a growth standard derived from a worldwide sample of children and based on the biological reality that environmental differences rather than genetic endowments are the principal determinants of disparities in physical growth is an important first step in carrying forward our duties and obligations to the human family.

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\*The six treaties that comprise this system are the Convention on the Elimination of All Forms of Racial Discrimination (in force since January 4, 1969); the International Covenant on Civil and Political Rights (in force since March 23, 1976); the International Covenant on Economic, Social, and Cultural Rights (in force since March 23, 1976); the Convention on the Elimination of Discrimination Against Women (in force since September 3, 1981); the Convention Against Torture (in force since June 26, 1987); and the Convention on the Rights of the Child (in force since September 2, 1990).

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# The WHO Multicentre Growth Reference Study: Planning, study design, and methodology

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) is a community-based, multicountry project to develop new growth references for infants and young children. The design combines a longitudinal study from birth to 24 months with a cross-sectional study of children aged 18 to 71 months. The pooled sample from the six participating countries (Brazil, Ghana, India, Norway, Oman, and the United States) consists of about 8,500 children. The study subpopulations had socioeconomic conditions favorable to growth, and low mobility, with at least 20% of mothers following feeding recommendations and having access to breastfeeding support. The individual inclusion criteria were absence of health or environmental constraints on growth, adherence to MGRS feeding recommendations, absence of maternal smoking, single term birth, and absence of significant morbidity. In the longitudinal study, mothers and newborns were screened and enrolled at birth and visited at home 21 times: at weeks 1, 2, 4, and 6; monthly from 2 to 12 months; and every 2 months in their second year. In addition to the data collected on anthropometry and motor development, information was gathered on socioeconomic, demographic, and envi-*

*ronmental characteristics, perinatal factors, morbidity, and feeding practices. The prescriptive approach taken is expected to provide a single international reference that represents the best description of physiological growth for all children under five years of age and to establish the breastfed infant as the normative model for growth and development.*

**Key words:** Anthropometry, child nutrition, child-hood growth, growth curves, growth references, infant feeding practices, infant growth

## Introduction

The World Health Organization (WHO), in collaboration with a number of institutions worldwide, is conducting a community-based, multicountry study to develop new growth references for infants and young children, the WHO Multicentre Growth Reference Study (MGRS). The approach taken to develop the new references is fundamentally different from that taken in the past. The new approach describes the growth of children whose care has followed recommended health practices and behaviors associated with healthy outcomes. The new curves may therefore be considered as prescriptive or normative references, as opposed to traditional descriptive references based on geographically representative samples of children, regardless of feeding or other behaviors. The MGRS is taking place in six countries representing the major world regions. This effort involves about 8,500 children and combines a longitudinal study from birth to 24 months with a cross-sectional study of children aged 18 to 71 months. This paper describes the planning, study design, methodology, study organization, and field logistics, and provides an overview of the different phases of the project from its inception in 1990 to its expected completion in 2010.

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

## Brief history and planning phase of the study

The origins of the MGRS go back to 1990, when the WHO Department of Nutrition established a Working Group to assess the growth patterns of breastfed infants and the relevance of such patterns to the development of growth reference data. The Working Group on Infant Growth was motivated by multiple reports in the literature documenting significant deviations between the growth patterns of healthy breastfed infants and that depicted by the US National Center for Health Statistics (NCHS)/WHO international growth reference. The report of the Working Group was published in 1994 [1, 2]. In its analyses, the Working Group also noted a number of technical problems in the NCHS/WHO international growth reference and concluded that these problems were sufficient to result in potentially harmful decisions in the nutritional management of individual infants and inaccurate population-based assessments.

The group members recommended that a new infant growth reference be developed and that subjects recruited for this purpose should come from populations whose infant-care practices approximated current health recommendations, especially those related to feeding. They further specified that participants in the proposed effort should come from multiple countries, unlike the NCHS/WHO international reference, which is based solely on US children who as infants were predominantly formula-fed [3]. The recommendations of the Working Group were subsequently endorsed by a WHO Expert Committee in 1993 [4, 5] and the World Health Assembly (WHA) in 1994 [6]. The scope and cost of such an ambitious undertaking called for international collaboration. The normative function of WHO placed it in a unique position to provide the leadership required to carry out a project of such complexity and global visibility.

## Development of the MGRS protocol

Following the WHA resolution, in 1995 a WHO Working Group on the Growth Reference Protocol was established, formed by pediatricians, nutritionists, human biologists, epidemiologists, and statisticians, to prepare a protocol for the development of a new growth reference based on an international sample of healthy breastfed infants [7–9]. For two years, this group established the framework that resulted in a protocol outlining a fundamentally new approach, prescriptive in nature. Rather than recommending an update of “how children are growing,” the group recommended that the reference describe “how children *should* grow.” This approach moved past the construction of a device for classifying and analyzing data and allowing the comparison of different populations, to the development of a *standard* (or as close to one as possible), i.e., a device

that embodies the concept of a norm or target and thus permits a value judgment. Drafts of the protocol were circulated to numerous external reviewers and presented in scientific meetings and review committees, and an initiative for raising the funds for the study was launched. Reactions from the scientific community as well as from donors were very supportive. However, the high cost of implementation of the study—about 10 million US dollars—represented for some donors too large an investment for a single project. Thus, efforts to raise the necessary funds to support the MGRS have been and continue to be an important aspect of the project’s implementation.

## Selection of study sites

In 1996, when the main features of the MGRS protocol were settled, we began the process of selecting sites for the implementation of the study. The need to identify sites in each of the six major geographic regions represented a second important challenge in the implementation of the MGRS. The process of selecting the study sites lasted two years and entailed evaluation of specific eligibility criteria for study subpopulations based on the study protocol. Following a presentation of the MGRS at the World Health Assembly, a number of countries expressed an interest in participating in the study. They were requested to send in responses to the checklist of criteria (table 1) documenting the source of the epidemiological data provided.

Since valid epidemiological data were unavailable for some sites to provide information for key items on the checklist, candidate groups were requested to conduct surveys to ascertain the feasibility of carrying out the MGRS. Four surveys were conducted in Asia, one in Africa, and one in the Middle East. The main objective of these surveys was to assess the growth of children living in affluent communities and identify socioeconomic characteristics associated with unconstrained growth in these populations. Information was also gathered on infant feeding patterns, mobility of the population, and other aspects relevant to the protocol. In addition to the survey information and other documentation, candidate sites were visited by members of the Working Group. The final decision about participation was made on the basis of the results of the surveys [10–12] or available epidemiological data from other sources [13], the geographic distribution of the candidate sites, the presence of collaborative institutions able to implement the MGRS protocol, and the availability of national or international funds. The description of the study sites in the six selected countries (Brazil, Ghana, India, Norway, Oman, and the United States) is presented in separate papers in this supplement [14–19] (fig. 1).



TABLE 1. Checklist for the assessment and selection of study sites

Primary criteria	Secondary criteria
<p><i>Socioeconomic status that does not constrain growth (i.e., epidemiological data showing low infant mortality rate and &lt; 5% prevalence of stunting, wasting, and underweight at 12–23 months of age)</i></p> <p>Description of socioeconomic characteristics of study subpopulation</p> <p>Infant mortality rate in subpopulation</p> <p>Rates of stunting, wasting, and underweight in subpopulation</p> <p>Estimated size of subpopulation</p> <p>Water sources in subpopulation (% with access to safe drinking water)</p> <p><i>Low altitude (&lt; 1,500 m)</i></p> <p><i>Low mobility of the target population to allow two-year follow-up of children</i></p> <p>Follow-up rates in previous longitudinal studies</p> <p>Census information on out-migration rates</p> <p><i>Minimum of 20% of mothers willing to follow feeding recommendations</i></p> <p>Percentage of mothers in subpopulation who breastfeed for 12 months or more</p> <p>Percentage of mothers in subpopulation who breastfeed exclusively for 4 months or more</p> <p>If these rates are not sufficient, evidence that they could be increased by the study team</p> <p><i>Existence of breastfeeding support system</i></p> <p>Existence of Baby-Friendly Hospitals</p> <p>Description of hospital practices</p> <p>Existence of breastfeeding support groups</p> <p>Presence of experienced lactation consultants</p> <p>Proportion of working mothers and length of maternity leave</p> <p><i>Local presence of qualified collaborative institutions</i></p> <p>Number and qualifications of scientists who will be involved in the study</p> <p>List of publications of the above scientists</p> <p>Description of previous research projects in relevant areas</p> <p>Availability of research assistants, interviewers, and data clerks</p> <p>Links with other national and international institutes</p> <p>Computing facilities</p> <p>Communications facilities</p>	<p><i>Rate of hospital deliveries. If home births are frequent, local teams need to prove that obtaining reliable anthropometric measures soon after birth is feasible and that the procedure for identifying newborns in the community does not result in selection biases</i></p> <p><i>Sufficient number of eligible births to enroll 300 newborns in 12-month period (at least 7–8 eligible births per week)</i></p> <p>Estimate of the rate of exclusions due to low socioeconomic status, smoking mothers, twins, preterms, etc.</p> <p>Estimated number of monthly births after exclusions</p> <p><i>Mean birthweight in study subpopulation</i></p> <p><i>Maternal height in study subpopulation</i></p> <p><i>Complementary feeding in study subpopulation</i></p> <p>Energy density of complementary foods</p> <p>Use of micronutrient supplements (e.g., iron, iodized salt)</p> <p><i>Health-related behaviors in study subpopulation</i></p> <p>Immunization rates</p> <p>Pediatric monitoring routines</p> <p><i>Environmental hazards</i></p> <p>Rate of diarrheal diseases</p> <p>Presence of significant nonmicrobiological contamination (e.g., exposure to radiation or toxic substances)</p> <p><i>Feasibility of implementing the study protocol</i></p> <p>Sample size calculations</p> <p>Number of hospitals to be surveyed</p> <p>Degree of collaboration from hospitals</p> <p>Size of geographic area for home visits</p> <p>Transportation facilities</p> <p>Location of study headquarters</p> <p>Data entry and management</p> <p>Estimated costs of study (interviewers, transportation, supervision, lactation support)</p> <p>Rate of refusals among subpopulation in previous studies</p> <p><i>Geographic distribution</i></p> <p>Existence of other candidate sites in the same geographic–ethnic unit</p> <p><i>Fundability</i></p> <p>Budget for four-year period</p> <p>Likelihood of availability of national or international funds</p>

### Preparations for launching the study

During late 1996 and early 1997, the Coordinating Centre, located at the WHO Department of Nutrition in Geneva, prepared the documentation and materials of the study in English, written in great detail, to be used at the study sites for the day-to-day implementation of the study. The documentation included the Manual of Operations, Measurement and Standardization protocols, study questionnaires and interviewer guides, and Data Management protocols (available on request). A training video on anthropometric techniques was prepared for the training and standardization of field staff [20], and a data management system was developed [21]. Study instruments were pretested

at the Brazilian site, which served as the pilot site. Study forms and interviewer guides were translated into Arabic, Norwegian, and Portuguese and back-translated into English to ensure that the content of the questions remained unchanged. The only documentation that was developed at a later stage, owing to a shortage of funding, was that related to the Motor Development Study [22]. The late initiation of this study made it impossible for the Brazilian site to participate in this MGRS component. The protocol for the Motor Development Study was pretested at the US site.

While site selection was ongoing, local investigators in confirmed sites proceeded with the recruitment and training of study teams. The planning phase at



FIG. 1. WHO Multicentre Growth Reference Study map

each study site is described in separate papers in this supplement [14–19]. Intensive exchanges took place between the Coordinating Centre of the MGRS at WHO and the sites to adapt the generic Manual of Operations to local circumstances and to prepare local staff for the launch of the study. Prior to the initiation of data collection, the Coordinating Centre trained and standardized local teams in anthropometric techniques [20], data management [21], and motor development assessment [22].

The planning phase of the MGRS culminated in the

enrollment of the first newborn in Pelotas, Brazil, on July 1, 1997. The initiation of data collection elsewhere followed, between 1999 and 2000, according to when sites were identified, local teams were trained and standardized, and funds were identified for the four-year implementation period. Data collection will be completed by November 2003, when the last newborn enrolled in India completes follow-up. The overall project timeline is shown in figure 2. The section that follows describes the study protocol and methods.

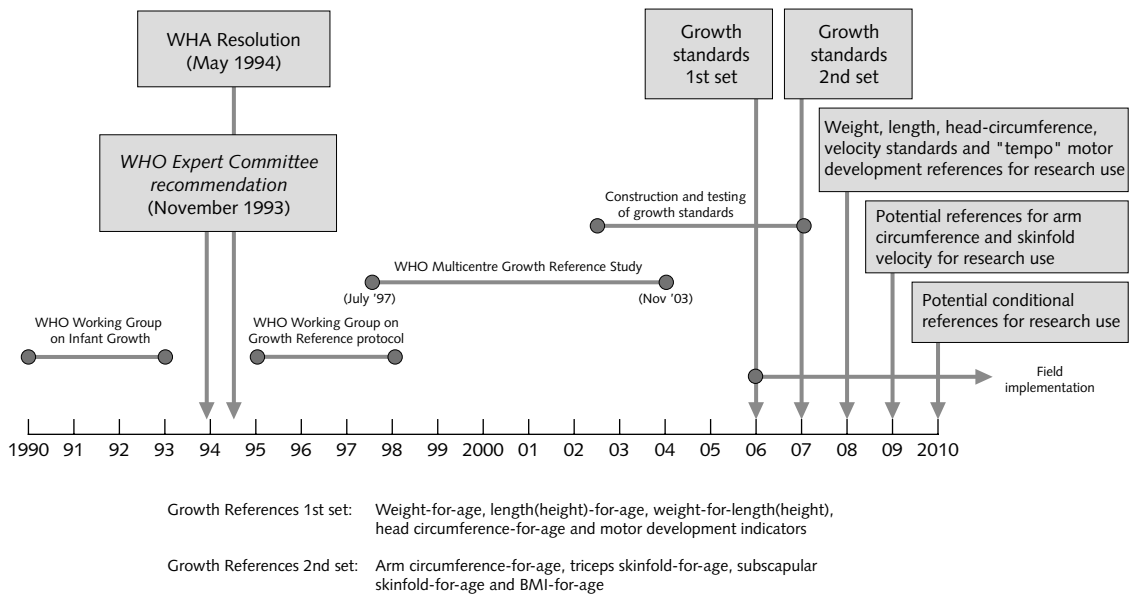


FIG. 2. Timeline of the new international growth references

## Methods

### Study design

The MGRS design combines a longitudinal study from birth to 24 months with a cross-sectional study of children aged 18 to 71 months. In the longitudinal study, cohorts of newborns were followed for the first two years, with frequent assessments of feeding practices and growth. A longitudinal design for the first two years was needed to provide lactation support to participating mothers, assess selection biases, and provide incremental measurements for the development of growth velocity references. Mothers and children were screened and enrolled at birth and visited at home 21 times: at weeks 1, 2, 4, and 6; monthly from 2 to 12 months; and every two months in the second year. Figure 3 presents the flow chart for the longitudinal study. Mothers enrolled at screening had a two-week period to consider and discuss their participation in the study with their families. Therefore, successful recruitment was determined at the week 2 home visit. Mothers who either refused outright, who posed important restrictions on their participation (“hidden refusals”), or who were found to be ineligible were replaced in the sample. Those who left the study after this point were considered dropouts and were not replaced.

A cross-sectional design was adopted for children aged 18 to 71 months to avoid the time and cost of conducting a longitudinal study in that age range, and also because growth in this age range is more linear than for younger children. Using 18 months as the lower age limit for the cross-sectional study allows an overlap of 6 months with the longitudinal study, which provides information on the transition from supine

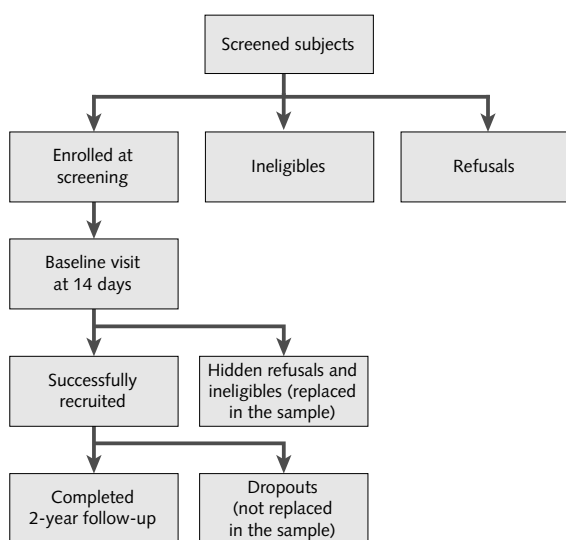


FIG. 3. Flow chart of longitudinal study

length to standing height and facilitates the joining of the two data sets. Although the curves will be built for children aged up to 60 months, data collection is extended to 71 months to provide reliable estimates of growth at 60 months (see below). Because of the large number of children required for the cross-sectional study, two sites with small population bases (Brazil and the United States) used a mixed-longitudinal design in which some children were measured two or three times [14, 19].

The MGRS is a population-based study with well-defined catchment areas from which mother–infant pairs are recruited: the cities of Davis, Muscat, Oslo, and Pelotas and selected affluent neighborhoods of Accra and South Delhi. In all sites, recruitment of infants for the longitudinal study took place in hospitals within 24 hours of birth. The number of participating hospitals was determined to ensure that 80% or more of the population in the designated catchment areas was screened for eligibility. For the cross-sectional study, the sampling strategy was developed according to the circumstances of each site, to provide a sample of children from the same population providing newborns for the longitudinal study [14–19].

A final important feature of the study design is that it pools samples of children who represent a diversity of ethnic backgrounds. The decision to include populations from the major world regions was supported by solid evidence showing that the growth patterns of well-nourished, healthy preschool children across the world are very similar [4, 8]. The surveys conducted as part of the selection process in the developing countries participating in the MGRS demonstrated that this was indeed the case [10–12]. The formulation of a truly international reference is likely to be more acceptable for global use than a reference developed with data obtained from a single country. This procedure averts political concerns that arise from using a single country’s child growth pattern as a worldwide standard.

### Eligibility criteria for study subpopulations and individual children

The eligibility criteria for study subpopulations were used for selecting the study sites (table 1). It was not necessary for the whole population from the study area to fulfill the criteria, since this restriction would probably have precluded the participation of most sites outside developed countries. These characteristics, however, had to be present among the subpopulations from which study participants were to be drawn. The mean birthweight in the target population was not included as an eligibility criterion; however, it was taken into account when selecting sites.

The eligibility criteria applied to individual mothers and children are listed in table 2. The absence of health, environmental, or economic constraints on

TABLE 2. Eligibility criteria for individual mothers and children

No health, environmental or economic constraints on growth
Mother willing to follow feeding recommendations
Term birth: gestational age $\geq 37$ completed weeks (259 days) and $< 42$ completed weeks (294 days)
Single birth
Absence of significant morbidity
Nonsmoking mother (before and after delivery)

growth was applied as a criterion in the selection of newborns. An objective of the surveys conducted prior to the implementation of the MGRS was to identify socioeconomic factors associated with unconstrained growth in the study subpopulation. Local criteria for screening newborns, based on parental education and/or income levels, were developed accordingly [10–12]. The feeding recommendations with which mothers were required to comply are summarized in table 3. Low-birthweight babies born at term were not excluded, since this restriction would have artificially distorted the lower centiles of the curves in the early months. The list of diagnoses of significant morbidity was developed in consultation with local neonatologists and pediatricians at each site [14–19]. Last, because smoking can affect both lactation performance and infant growth [23–25], as well as birthweight [26], maternal smoking before or after delivery was made an exclusion criterion.

The eligibility criteria were similar for the longitudinal and cross-sectional studies, with the exception of the feeding recommendations, where a minimum duration of three months of any breastfeeding was imposed as an inclusion criterion for the cross-sectional study sample.

### Sample size

The precision of growth chart centiles is determined by

several factors, of which the most important is sample size. Other relevant factors include study design (cross-sectional versus longitudinal), the timing of measurements, and the method of curve fitting. Four criteria were used to set the sample size for the MGRS: the precision of a given centile at a particular age, the precision of the slope of the median curve over a given age range, the precision of the median curve overall and the influence of data at particular ages, and the precision of the correlation between measurements in the same subjects at different ages. The last criterion is relevant for velocity references. Sample sizes were calculated for each of these four criteria, and it was found that, for each sex, a sample size of 200 for the longitudinal study and 200 per three months for the cross-sectional study would provide adequate precision. These sample sizes were to be obtained by combining data from the six sites.

The sample size calculations yielded the finding that the first few measurements, particularly birthweight, have high variance, whereas between one and four years the variance is low. In addition, limiting the study to children under five years results in increased imprecision during the fifth year. To address the imprecision of the curves at the extremes, birthweight was oversampled and the upper age limit was raised. The sample at birth was increased fourfold, and an upper limit of 71 completed months for the cross-sectional study was implemented to improve the precision of the curves throughout the whole age range of interest.

In the longitudinal study, to obtain 400 children of both sexes, 70 compliant children per site were required to complete the two-year follow-up. The number of newborns to be recruited initially depended on the proportions expected to remain compliant (with feeding recommendations and smoking restrictions) until the age of two years. Based on calculations made from available epidemiological data, the recruitment of a target sample size of 300 newborns per site was set, the only exception being the US site, where the recruitment target was 200 newborns because the expected

TABLE 3. Operational criteria and definitions for compliance to feeding recommendations

Criteria	
Exclusive or predominant breastfeeding for at least 4 months (120 days)	
Introduction of complementary foods by the age of 6 months (180 days)	
Partial breastfeeding to be continued for at least 12 months (365 days)	
Definitions	
Exclusive breastfeeding	The infant has received only breastmilk from its mother or a wet nurse, or expressed breastmilk, and no other liquids or solids with the exception of drops or syrups consisting of vitamins, mineral supplements, or medicines
Predominant breastfeeding	The infant's predominant source of nourishment has been breastmilk. However, the infant may also have received water and water-based drinks (e.g., sweetened and flavored water, teas, infusions); fruit juice; oral rehydration salts (ORS) solution; drop and syrup forms of vitamins, minerals and medicines; and ritual fluids (in limited quantities). With the exception of fruit juice and sugar water, no food-based fluid is allowed under this definition

compliance was higher. This total recruitment target fulfilled the requirement that the sample size at birth be at least four times larger than the 400 required at older ages.

To provide similar measurement densities at 18 to 71 months, the cross-sectional study was designed to include the same number of children (70 per three-month period), with each child measured once. The period from 18 to 71 months covers 18 three-month periods, so the nominal sample size required was  $70 \times 18 = 1,260$  children per site. Adding 11% for refusals gave a round sum of 1,400 subjects per site (78 per three-month period). This target sample size was lower for the two sites that used a mixed-longitudinal design, since some children at these sites were measured more than once. Moreover, because the MGRS protocol called for minimizing the number of children participating in both the longitudinal and the cross-sectional samples, the target age interval for the cross-sectional study at the US site was restricted to 27 to 71 months [19]. To fill the gap created by the absence of children in the age range from 24 to 26 months in the US sample, the site in Norway recruited an extra 70 children in this age range.

When the longitudinal cohorts and cross-sectional samples for the six sites are combined, the total MGRS sample size is about 8,500 children. The high compliance and low attrition rates that have been experienced ensure that the new growth curves will be based on a sample size that exceeds the minimum required sample of 200 children for each sex and age group.

### Information collected and study questionnaires

The study forms were centrally prepared by the WHO Coordinating Centre accompanied by interviewer guides with detailed instructions for training and field use. The questionnaires included closed questions with precoded answers. In addition to the data collected on anthropometry and motor development, information was gathered on socioeconomic, demographic, and environmental characteristics; perinatal factors; morbidity; and feeding practices. The anthropometric measurements, described in detail in a separate paper [20], included weight, length, height (in the cross-sectional study only), head and arm circumferences, triceps and subscapular skinfold thicknesses, and parental weight and height. Motor development data covered the acquisition of six milestones: sitting without support, hands-and-knees crawling, standing with assistance, walking with assistance, standing alone, and walking alone. The motor development protocol is described in detail in a separate paper in this supplement [22].

All questionnaires were kept as short as possible to improve responsiveness and sample retention. Therefore, all candidate questions were scrutinized initially

to ensure that they served at least one of the following purposes: establishing eligibility (e.g., socioeconomic status, intention to breastfeed); describing the sample (e.g., demographic and environmental variables); standardizing findings across centers (e.g., parental height); planning breastfeeding support (e.g., initiation of breastfeeding); assessing continued eligibility (e.g., feeding practices, illnesses); guiding future use of references (e.g., vitamin and mineral supplements); or assessing possible selection biases (e.g., maternal work).

A number of different study forms were used in the longitudinal study:

- » A screening form, administered at birth, was used to evaluate eligibility and recruit mothers and newborns. It included data on specific exclusion criteria, such as those related to the family's socioeconomic status, the mother's intention to breastfeed, the newborn's gestational age, and maternal smoking behavior.
- » A breastfeeding-in-hospital form, which described breastfeeding initiation, timing, and pattern.
- » Four breastfeeding-at-home forms were used at weeks 1 and 2 and months 3 and 6. Information was collected on the establishment of lactation, problems experienced in the first two weeks (such as delayed onset of milk production and breast infections), and practices with potentially adverse influences on continued lactation (such as pacifier use and contraception).
- » A baseline form administered at the day 14 visit collected information on socioeconomic, demographic, and environmental factors; pregnancy history; and parental anthropometry.
- » The follow-up questionnaire was administered at each of 20 follow-up visits to record detailed information on feeding patterns (including the 24-hour dietary recall for the preceding day); maternal and child morbidity; use of vitamin and mineral supplements; maternal employment, smoking, and weight; and child anthropometry.
- » For motor development, as many as 14 forms were completed in months 5 to 24, but children who could walk independently before the age of 24 months required the completion of fewer forms. All six milestones were assessed on each occasion.
- » An end-of-participation form specifying the reason for ending participation was completed for all subjects who were recruited at the initial screening. Possible reasons included ineligibility or refusal established at the day 14 visit, reasons for dropping out from the study on a later occasion, and the end of follow-up for those who successfully completed the study.
- » A 12-month-visit questionnaire was administered to mothers who, although eligible, did not intend to breastfeed; who refused to participate in the study

at any stage; or who dropped out of the study before 12 months for reasons other than child illness. The form gathered selected anthropometric data and information related to the child's morbidity and feeding history.

The cross-sectional study used three study forms:

- » A screening form collected information used to establish eligibility on variables similar to those used in screening for the longitudinal study.
- » A survey form covered socioeconomic and demographic factors, child feeding history and morbidity, and parental and child anthropometry.
- » In the context of the mixed-longitudinal design, one or two follow-up forms (abbreviated versions of the survey form described above) were used in Brazil and the United States to gather data on anthropometry and child morbidity in the intervals between visits.

### Quality control

Rigorous scientific standards have been applied to this complex, multicountry, field-based project. This section summarizes the main measures taken to ensure data quality, most of which are detailed further elsewhere in this supplement [20–22]. Quality control measures included the following:

- » Pilot testing of study protocol;
- » Use of pretested, standardized data collection forms and detailed interviewer guides;
- » Translation into local languages and back-translation of questionnaires and other forms;
- » Careful selection, thorough training, and close supervision of staff;
- » Regular visits to study sites;
- » Training on anthropometric measurements and motor development assessment by international experts with annual site visits by the experts for standardization and/or retraining purposes;
- » Regular standardization sessions throughout data collection, with assessment of intra- and interobserver reliability [20, 22];
- » Specially designed and highly reliable measuring equipment that was calibrated frequently [20];
- » Coordination meetings and staff exchanges among sites;
- » Continuous data quality assurance from the point of data collection (independent measurements by two standardized observers [20]), through all stages of data management to their incorporation into the MGRS master files [21];
- » Repetition of 10% of all interviews on the telephone;
- » Continuous central monitoring of the timing of visits (including delayed, advanced, or missed visits), frequency of repeated measurements, missed measurements, investigation of outliers, terminal digit preference, and results of anthropometric and motor

development standardization sessions.

The monitoring of data quality was effective in identifying deviations from MGRS standards, and early, appropriate remedial measures were taken.

### Data management and analysis

The MGRS data management system is described in full elsewhere in this supplement [21]. Data were entered concurrently with data collection, verified and validated at the study sites, and sent on a monthly basis to the Coordinating Centre at WHO. MGRS master files were consolidated and ongoing data quality control analyses were carried out at the Coordinating Centre to monitor study implementation and assess adherence to the study protocol.

All data analyses will be conducted at the Coordinating Centre. The Coordinating Centre will be responsible for constructing the new growth references using state-of-the-art statistical techniques. In preparation for the analysis phase, a review of the different methods for the construction of distance, velocity, and conditional growth references was recently conducted by WHO. A full description of the 30 methods reviewed is beyond the scope of this paper. The review document was circulated for external peer review and discussed at a WHO meeting of an ad hoc statistical advisory group. The group identified several criteria for assessing the different methods (e.g., distributional assumptions, curve fitting, age handling, and model simplicity) and, based on these criteria, selected methods to be tested for the growth parameters included in the MGRS. Model diagnostic tools for assessing the appropriateness of the selected methods were also identified. Given the numerous sets of growth reference data that will be produced—including novel references based on circumferences, skinfolds, and growth velocity—the construction and testing of the various references promises to be a complex and challenging task.

### Methodological issues

An important concern when proposing a reference based on recommended practices is how such restrictions may affect other characteristics of the reference sample. For example, mothers who choose to breastfeed exclusively or predominantly may also present behaviors other than feeding choices that influence child growth. If a reference population is overly homogeneous, the distribution of values will be too narrow, resulting in statistically based cutoffs that are closer to the mean than would occur in an appropriately heterogeneous reference population.

In response to the concern that the prescriptive approach taken for the development of the new reference might result in an excessive degree of sample selectivity, measures were built into the study protocol

to minimize bias and assess the potential influence of selection bias on the outcomes of interest:

#### **Measures to minimize inappropriate sample selectivity**

- » *Implementation of the study in sites where at least 20% of the mothers in the study subpopulation were likely to comply with the feeding recommendations of the study (tables 1 and 3).*
- » *Application of operational definitions of feeding recommendations that would allow a greater proportion of children to be included in the growth reference data set.* Some flexibility in the operational definitions was expected to reduce selectivity problems with the cohorts to be followed and to lessen economic and logistic constraints. Furthermore, available evidence and analyses conducted during development of the MGRS protocol indicated that there were small, if any, differences between the growth of exclusively and predominantly breastfed infants in the first six months of life [8, 27] and that postnatal growth did not appear to be very sensitive to the differential timing of introduction of complementary foods among healthy infants living in safe environments [9, 28]. It was therefore decided that, for the purpose of constructing the growth curves, the feeding criteria to be used would be those listed in table 3. However, at the field level, mothers participating in the MGRS would be advised to breastfeed their infants exclusively for as close as possible to six months, with introduction of complementary foods by the six-month visit.
- » *Provision of intensive breastfeeding support to participating mothers to enhance compliance and reduce selection bias by ensuring a high level of compliance with feeding recommendations.* To allow a high proportion of mothers wishing to breastfeed to actually do so, lactation counseling was made an essential part of the MGRS. At each site, trained counselors visited participating mothers frequently in the first months after delivery to help successful breastfeeding initiation and to advise on subsequent problems. The first visit took place within 24 hours of delivery, and subsequent visits were made at 7, 14, and 30 days, and then monthly thereafter until at least the sixth month. Additional visits were carried out whenever feeding problems occurred. A 24-hour hotline also was made available to mothers for emergency support. Mothers also received advice on complementary foods—with emphasis on energy density, feeding frequency, and micronutrient content—according to locally adapted complementary feeding guidelines. Descriptions of the local lactation counseling teams and complementary feeding guidelines are provided elsewhere in this supplement [14–19].

Compliance with feeding recommendations was monitored centrally throughout the study, and lacta-

tion counseling was strengthened as required. Preliminary results strongly suggest that the above measures have been effective and that compliance rates across sites have been high, minimizing concerns about the selectivity of the MGRS sample.

#### **Measures to assess sample biases**

Two key measures were included in the study protocol to permit the assessment of possible selection biases affecting the sample:

- » *Follow-up of the entire cohort independent of compliance status.* This allows the comparison of the patterns of growth of children whose mothers complied with the feeding and smoking recommendations with those who entered the study but whose mothers subsequently failed to comply with the recommendations of the study.
- » *The 12-month study.* This substudy involved visiting a sample of eligible nonparticipating infants on their first birthdays to compare their attained weights and lengths with those of the cohort children. Four categories of children were included in this substudy: those whose mothers refused to participate at screening; those whose mothers did not intend to follow the feeding recommendations at screening; those excluded at the day 14 visit because the mother had started feeding other milks; and those who dropped out of the study before the age of 12 months.

## **Study organization and field logistics**

### **Study organization**

The study organization is presented in figure 4. The study was initiated, coordinated, and managed by the Department of Nutrition of WHO, where the MGRS Coordinating Centre was located. The Steering Committee consisted of WHO staff from the Coordinating Centre, the investigator(s) at each participating site, and representatives from the United Nations University and UNICEF. The Steering Committee met four times throughout implementation of the study to review the progress of the study, ensure uniformity of data collection from the different sites, and discuss substan-

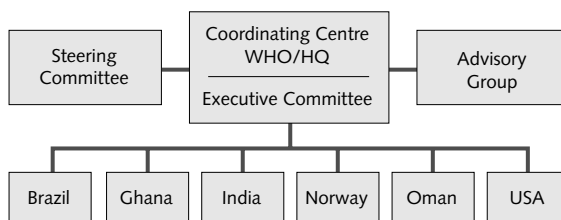


FIG. 4. Study organization

tive issues that arose. The study structure included an Executive Committee, formed by five members of the Steering Committee, which reviewed the progress and problems of the study on a regular basis and resolved substantive issues that arose from the implementation of the study. All local adaptations made to the MGRS protocols or issues related to the technical conduct of the study required review and approval by the Executive Committee. The Executive Committee also decided on the selection of study sites, the continuing participation of selected sites, and issues related to the inclusion or exclusion of data in the pooled international data set. An Advisory Group, formed by internationally recognized experts in anthropometry, epidemiology, statistics, nutrition, and human biology, provided technical advice to the Coordinating Centre, Executive Committee, and Steering Committee. Policies related to the dissemination of results and data ownership were developed prior to initiation of the study.

### Field logistics

Fieldwork was undertaken by approximately 200 staff members working in different teams covering the areas of coordination, screening, lactation counseling, follow-up, and cross-sectional study. Data management teams were also present in each site. Further information on the study teams and other aspects of field logistics is presented in the papers describing the implementation of the study at specific sites [14–19]. For those interested in replicating the study elsewhere, the Manual of Operations is available on request from the first author.

### Ethical issues

The study complied with the International Ethical Guidelines for Biomedical Research Involving Human Subjects [29] and received ethical approval from international, national, and local ethical review committees. Written informed consent was obtained from the parents of all children enrolled in the study.

### Discussion

Growth references for infants and young children are among the most widely used instruments in public health and clinical medicine. In collaboration with a number of institutions worldwide, WHO has undertaken a major initiative to develop new growth references for infants and young children. The approach taken avoids the limitations imposed by descriptive designs that portray growth characteristics of geographically defined samples that are limited in their definition of health by relying only on the absence of overt disease at the time of measurement. Although

the absence of disease remains a requirement in the WHO approach, it is no longer a sufficient criterion. The adopted strategy also requires that the reference population be defined on the basis of a number of other parameters centered on normative behaviors and other characteristics strongly associated with healthy outcomes. Furthermore, it requires that an international sample of children be used.

The MGRS is an ambitious undertaking, but the goals established on initiation of the study have been achieved successfully. The rigor with which the protocol was implemented and the data assurance procedures that were put in place have yielded a data set of outstandingly high quality. Factors that contributed to success were modern communication systems that allowed close and frequent contact between the Coordinating Centre and the sites, the continuous monitoring of data quality, the early detection and adoption of remedial measures for identified problems, and ongoing standardization within and between sites. The path to success, however, was not free of challenges.

Initial important challenges were the selection of study sites and the need to raise funding from external donors. The high cost of the study required funding from multiple donors and was largely responsible for the staggered initiation of the study in the six sites, making its management at times difficult. The high level of collaboration and uniformity that was required by a multicenter, multicultural study of this nature also presented major challenges. Close central monitoring was applied to ensure adherence to study procedures to guarantee the collection of comparable data. During the seven years of data collection, the Coordinating Centre maintained almost daily contact with the local investigators and data managers through modern communication systems and conducted frequent site visits to answer queries and assist in the data collection process. Locally, periodic coordination meetings also were conducted. There were also substantial cross-site staff exchanges to assist in lactation support, data management, data quality assurance, or motor development assessments. This created a sense of international teamwork that contributed significantly to the success of the MGRS.

The development and testing of the various growth references promises to be a complex and challenging task. This expectation is borne out by recent national experiences of a similar nature. The wealth of data being collected will allow not only the replacement of the current international references on attained growth (weight-for-age, length/height-for-age, and weight-for-length/height) but also the development of new references for triceps and subscapular skinfolds, head and arm circumferences, and body mass index. The longitudinal nature of the study will also allow the development of growth velocity curves. Health-care providers will not have to wait until children cross an



attained growth threshold to make the diagnosis of under- or overnutrition, because velocity references will enable the early identification of children in the process of becoming under- or overnourished. Similarly, the documentation of the timing of motor milestones in the longitudinal component will further enhance the value of these data by providing a unique link between physical growth and motor development. The main drawback of the new growth curves, however, is that they will cover only children up to five years of age. The need to expand this effort to older children is evident.

Ahead of us lies the implementation of the new growth references at the country level. In preparation for this phase, we recently conducted a worldwide survey of national practices in the use and interpretation of growth charts that highlighted the interest many countries have in adopting the new growth references when they become available [30]. The results from the survey also indicate that the process of replacing existing growth charts and retraining fieldworkers in the uses and interpretation of new ones must go beyond the simple change of charts, to revisiting growth monitoring practices as a whole. Intensive training efforts at all levels will be required to overcome the difficulties health workers experience with the use and interpretation of growth curves and to disseminate knowledge about effective interventions to prevent or treat either excessive or inadequate growth at both the individual and the population levels. Undoubtedly these future efforts will require a number of partnerships for their successful implementation.

Thirteen years have passed since the seed for this effort was planted. It is reasonable to ask whether the preparatory phases could have been shortened. We think that the long preparatory activities, including several Working Groups and review committees, have been decisive for the successful implementation of the study.

It is unlikely that the high level of uniformity would have been achieved in such a complex multicultural project without this investment of time and effort.

The completion of weight, length, and head circumference references is anticipated before the end of 2005. The remainder of the references should be ready by 2006 (fig. 2). Of particular concern is a smooth global transition to the new references by field testing and/or use simulation of provisional references that take into account the diverse settings in which individual and population assessments occur in both developed and developing countries. This will be accomplished before the growth references are released.

The MGRS will provide a technically sound set of tools for assessing the growth and development of children worldwide for many years to come. An important characteristic of the new reference is that it makes breastfeeding the biological "norm" and establishes the breastfed infant as the normative model. Health policies and public support for breastfeeding will be strengthened when breastfed infants become the reference for normal growth and development. By prescribing the nature of the sample, the recommended approach will provide a single international reference that represents the best description possible of growth for all children less than five years of age and approximates the closest attainable "standard" of physiologic growth.

Full details about the procedures and methods, such as those contained in this supplement, are often not available in the literature. This study will be an important source of information for years to come about child growth and development and infant nutrition. It is therefore important to have a faithful record of the planning, methodology, and implementation, particularly for the benefit of those who may not have been directly involved with the MGRS but will be using the new growth charts in the near future.

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# Measurement and standardization protocols for anthropometry used in the construction of a new international growth reference

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## Abstract

*Thorough training, continuous standardization, and close monitoring of the adherence to measurement procedures during data collection are essential for minimizing random error and bias in multicenter studies. Rigorous anthropometry and data collection protocols were used in the WHO Multicentre Growth Reference Study to ensure high data quality. After the initial training and standardization, study teams participated in standardization sessions every two months for a continuous assessment of the precision and accuracy of their measurements. Once a year the teams were restandardized against the WHO lead anthropometrist, who observed their measurement techniques and retrained any deviating observers. Robust and precise equipment was selected and adapted for field use. The anthropometrists worked in pairs, taking measurements independently, and repeating measurements that exceeded preset maximum allowable differences. Ongoing central and local monitoring identified anthropometrists deviating from standard procedures, and immediate corrective action was taken. The procedures described in this paper are a model for research settings.*

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Mention of the names of firms and commercial products does not imply endorsement by the United Nations University.

**Key words:** Anthropometry, growth curves, growth references, height, length, methods, skinfold, weight

## Introduction

The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) was undertaken to generate new growth curves for assessing the growth and development of infants and young children from around the world. The children included in the study came from six countries: Brazil, Ghana, India, Norway, Oman, and the United States. The methodology and eligibility criteria for the study have been described elsewhere in this supplement [1]. Identical, rigorous data collection procedures were followed in all sites in order to minimize measurement error and to avoid systematic differences among sites.

Variability in infant and child measurements can result from a number of influences: the setting in which the measurements are taken; stomach and bladder volume (in the case of weight); diurnal variation (in length/height); the behavior and cooperation of the child being measured; the accuracy and precision of the instruments; the anthropometrist's technical capacity (training, experience, and reliability), fitness, and mood; and the methods of data recording (reading, writing down). Appropriate training and continued standardization, adherence to specified methods and procedures, and monitoring of data quality are essential to reduce measurement error and minimize bias in multisite studies. The purpose of this article is to describe the measurement protocols and routine standardization sessions that were used in the MGRS. The study protocols and quality control procedures can be applied in research settings without substantially increasing costs or complicating logistics.

## Selection and training of anthropometrists

The field staff collecting anthropometric data in the

MGRS (referred to herein as observers or anthropometrists) had to have at least secondary school education, be motivated, write legibly, speak the local language, and be able to interact appropriately with the high-socioeconomic-status families that were targeted for the study. All candidates received standardized training, and only those who met the MGRS performance criteria were retained for the study.

The measurement procedures and training guidelines were prepared by the MGRS Coordinating Centre at WHO in Geneva, based on best practices recommended in anthropometry manuals and in the literature [2–8]. The initial training of anthropometrists at each site was carried out by an experienced anthropometrist following the procedures detailed in the MGRS protocol. All anthropometrists were trained to interview mothers, complete the study questionnaires, measure children as described in the protocol, avoid digit preference or transposition of numbers, record measurement values immediately after reading them, and write legibly to reduce mistakes during data transfer. Strict adherence to the measuring techniques and recording procedures was emphasized. Instructions were also provided on handling uncooperative children, taking into account cultural factors and individual mothers' sensitivity to their babies' crying.

Early in the study, four anthropometrists were trained and standardized against an expert designated by WHO as lead anthropometrist for the MGRS (W.C.C.) in a cross-site session held in Rotterdam, the Netherlands. Two of the participants were study supervisors from sites, one was a member of the Coordinating Centre, and the fourth (J.V.dB.) became the second WHO-designated lead anthropometrist for the MGRS.

Following the initial training and before the start of data collection, the anthropometrists in each site were standardized against one of the two WHO lead anthropometrists. The anthropometrist with the best performance at this session was designated "local lead anthropometrist" and was responsible for retraining teammates who deviated from MGRS techniques, and for training newly recruited anthropometrists later in the study. A WHO lead anthropometrist visited each site annually to ensure that identical methods were followed throughout the seven years of the study. The measurement procedures followed in the MGRS were documented on videotape (available to readers on request from the first author) and viewed during training and regularly thereafter to reinforce the key features of the measurement protocols.

## Standardization

Given the objectives of the MGRS, standardization within and among sites was a key aspect of the study [1]. An important goal of standardized training is to

enable observers to measure accurately, that is, without bias. To achieve this, observers need to be trained to obtain measurements that are on average equal to the values measured by an expert anthropometrist who is considered the "gold standard." The degree of accuracy can be assessed in a test–retest study in which several children are measured by both the expert and the observer, and bias is calculated as the average deviation of the observer's mean measurement values from those of the expert.

It is equally important that the measurements taken be precise, that is, reproducible. High precision is possible only if measurement procedures are highly standardized. Precision is assessed on the basis of differences between replicate measurements taken on several subjects in the test–retest study. The most commonly used parameter for lack of precision is the technical error of measurement (TEM) [9].

Following the initial standardization session and throughout the data collection phase, each site conducted standardization sessions bimonthly (every two months) that coincided once a year with the visit of the WHO lead anthropometrist. The purpose of these sessions was to identify anthropometrists deviating from the MGRS procedures. Corrective actions, such as retraining, were taken whenever deviations in measurement techniques were noted.

The initial standardization session used groups of 20 children for each set of measurements and took five or six days to complete, whereas the bimonthly sessions required only 10 children and could be accomplished in two or three days. At the initial session, the observers were standardized against the WHO lead anthropometrist, who served as the gold standard, whereas the bimonthly sessions used the observers' overall mean of each anthropometric variable as the gold standard. The longitudinal screening and follow-up teams were standardized separately because of the different age groups and settings involved: the screening teams measured newborns in maternity wards, whereas the follow-up teams measured infants and older children during home visits.

Analyses of accuracy and precision were performed soon after the standardization sessions using a centrally prepared Excel spreadsheet program with standard formulas for calculating relevant statistics [9–14]. To illustrate how the observers' performance was assessed, table 1 presents length data from the Rotterdam session, in which 25 children participated. For precision (TEM), the observers' performance compared well with that of the lead anthropometrist and the overall mean. This demonstrated that the participants in the session followed consistent techniques in measuring length and obtained reproducible values. The sign test for precision assesses the "measurement effect," where an observer's retest measurements may be systematically lower or higher than his or her own first measurements

TABLE 1. Precision and accuracy from the standardization session in Rotterdam: length data

Variable	WHO lead anthropometrist	Observer 1	Observer 2	Observer 3	Observer 4	Overall mean
TEM <sup>a</sup> (cm)	0.34	0.48	0.33	0.39	0.35	0.38
F test						
Lead anthropometrist <sup>b</sup>	—	.10 < <i>p</i> < .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25
Overall mean <sup>b</sup>	<i>p</i> > .25	.10 < <i>p</i> < .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25
Sign test <sup>c</sup>	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05
Bias (cm)						
Lead anthropometrist <sup>d</sup>	—	-0.49	-0.21	-0.15	-0.15	-0.15
F test <sup>e</sup>	—	<i>p</i> < .01	.01 < <i>p</i> < .05	.05 < <i>p</i> < .10	<i>p</i> < .01	<i>p</i> < .01
Sign test <sup>f</sup>	—	<i>p</i> < .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05
Overall mean <sup>d</sup>	0.21	-0.33	-0.00	0.08	0.07	
F test <sup>e</sup>	.10 < <i>p</i> < .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25	<i>p</i> > .25
Sign test <sup>f</sup>	<i>p</i> > .05	<i>p</i> < .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05	<i>p</i> > .05

a. Technical error of measurement:  $\sqrt{(\sum d_i^2/2n)}$ ; where  $d_i$  is the difference between the  $i$ th subject's test and retest measurements by the observer and  $n$  is the number of measured subjects.

b. F ratio for precision: Observer  $\sum d_i^2$ /Lead anthropometrist  $\sum d_i^2$ . When overall mean is the gold standard,  $d_i$  in the denominator is the difference between the  $i$ th subject's overall mean of test and overall mean of retest measurements.

c. Precision sign test: binomial proportion  $p$ , where  $p = x/n$ , and  $x$  is the frequency of the observer's retest scores that are higher (or lower) than the corresponding test scores. Significance is based on exact confidence limits for proportions when  $n \leq 75$  (see Table B.11 in Daly and Bourke [10]).

d. Average bias: Observer  $\sum \Delta_i/n$ ; where  $\Delta_i$  is the difference between the observer's mean and the lead anthropometrist's (or overall) mean measurement for the  $i$ th subject.

e. F ratio for bias: Observer  $\sum \Delta_i^2$ /lead anthropometrist's or overall means'  $\sum d_i^2$  (same denominator as the precision F ratio).

f. Bias sign test: binomial proportion  $p$ , where  $p = x/n$ , and  $x$  is the frequency of the observer's means that are above (or below) the lead anthropometrist's or overall mean. Significance is based on exact confidence limits for proportions when  $n \leq 75$  (see Table B.11 in Daly and Bourke [10]).

[15]. No such measurement effect was evident for any participant in this session. For accuracy, the observers showed a systematic tendency toward negative bias compared with the lead anthropometrist; consequently, the techniques for measuring length were reviewed. As expected, the negative bias was not evident when compared with the overall mean, except for observer 1. Both the F test and the sign test for accuracy are useful. The sign test checks whether poor accuracy results from systematic or occasional bias [10, 15]. For example, the average bias could be low and nonsignificant when a large deviation overwhelms smaller but systematic differences. In this case, the sign test, but not the F test, would indicate bias. For this session, only one observer's bias was systematic, and this was corrected by retraining.

The results of the bimonthly standardization sessions were sent to the Coordinating Centre soon after their completion. The average TEMs for each site were plotted to monitor overall performance over time, as figure 1 illustrates (for length). In general, the TEMs were highest at the start, and following a pattern that is consistent for all the other measurements, precision improved as the observers gained experience. Once stabilized, the average TEMs remained low, reflecting the high precision of the measurements taken by the study teams. When sending the bimonthly results to the

Coordinating Centre, sites reported on extraneous circumstances that affected the observed performance. For example, figure 1 shows a peak in TEM for the eighth bimonthly session in Brazil, when the children involved were particularly uncooperative. On the rare occasions when a problem identified in the sites needed external assistance, the WHO lead anthropometrist visited the affected site to retrain the observers. This was the case for triceps skinfold measurements at one site.

## Anthropometric procedures

### Measuring equipment

All study sites used the same measuring equipment. The instruments needed to be highly accurate and precise, yet sturdy and portable enough to be carried back and forth on home visits.

Length was measured with the Harpenden Infantometer (range, 30–110 cm for portable use, with digit counter readings precise to 1 mm). Because the MGRS protocol specified measuring length in the cross-sectional study for children aged 18 to 30 months (to allow a precise estimation of the systematic difference between length and height), a longer-than-usual infantometer was specially built for the study.

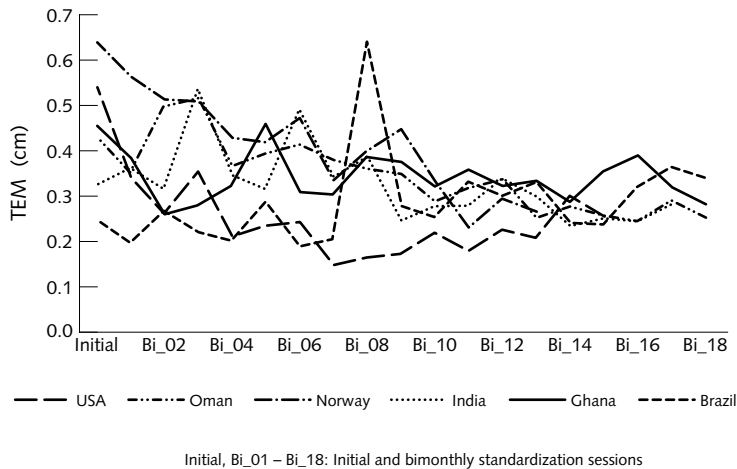


FIG. 1. Technical error of measurement (TEM) for length at initial session and up to 18 bimonthly (every two months) standardization sessions in the study sites

The Harpenden Portable Stadiometer (range, 65–206 cm, digit counter reading) was used to measure both adult and child heights. At the request of WHO, the manufacturer designed a wooden base to replace the heavy carrying case that serves as a mount for the traditional portable stadiometer. This adaptation decreased the weight of the packaged stadiometer by about 7 kg and reduced the time required to assemble it.

A self-retracting, 0.7-cm-wide, flat metal tape with blank lead-in strip (range, 0–200 cm, calibrated to 1 mm) was used to measure circumferences. Metal tapes were chosen because they are more robust and accurate and stay in a single plane around the head. They were replaced on a regular basis when the grading marks faded. The Holtain/Tanner-Whitehouse Skinfold Caliper (jaw face area, 35 mm<sup>2</sup>; pressure between the jaws,  $10 \pm 2$  g/mm<sup>2</sup>; range, 0–40 mm; calibrated to 0.2 mm) was used to measure skinfolds.

To measure weight, we used portable electronic scales that have taring capability and are calibrated to 0.1 kg (UNICEF Electronic Scale 890 or Uniscale). Ideally, newborns should be measured with a scale of higher precision (within 10 g). However, the advantages of the Uniscale greatly outweighed the disadvantage of its lower precision for young babies. The scales were satisfactorily pilot tested in the Brazilian site; they were easy to use and transport, and tared weighing allowed the infants to remain in their mothers' arms where they were more calm and relaxed. This was important for the mothers' positive perception of the study and, thus, participation. The scale's electronic display decreased the observer measurement error. In cold climates, the infants could be wrapped up in a blanket for weighing after the weight of the blanket had been tared. Another advantage of the Uniscale was that it allowed the mother's weight to be recorded at each visit, thus permitting the collection, at no extra cost, of weight

data for lactating women.

The equipment was calibrated regularly, usually daily before the home or hospital visits. The scales were calibrated with locally available standard weights over the full weight range, and tared weighing was simulated. The infantometer and stadiometer were calibrated by using metal rods of known lengths. The skinfold calipers, being particularly fragile, were checked before each use with calibration blocks of various widths for accuracy and to ensure that the needle moved smoothly and continuously with the opening of the caliper jaws.

#### Anthropometric data collection

Measurements were taken and recorded by two trained and standardized anthropometrists. Both the questionnaire forms and the standard procedures were designed to ensure that each observer read and recorded measurements independently of the other. At each session, the two exchanged roles as "leading" and "assisting" observers. The role of the assisting observer was to help position the child correctly while the leading observer took and recorded measurements. The first observer measured and immediately recorded each of the measurements, and they then exchanged roles so that the second observer could also take the full set of measurements. They then compared their values to ensure that duplicate measurements were within the maximum allowed differences. Any measurements falling outside the maximum allowed differences were repeated by both observers and entered in designated boxes on the data recording sheet. No more than two remeasurements were allowed (i.e., a maximum of three duplicate measurement sets for a given anthropometric parameter at any one visit). All recorded measurements were entered into the computer. The final value to be

used for the construction of the growth curves will be the average of the last pair of measurements. In the rare cases (< 0.1%) when the child was judged to be too agitated for reliable duplicate measurements to be taken, only one set of measurements was recorded. In practice, it was observed that large differences owing to reading or recording errors were resolved by a first repeat measurement. However, when the babies were uncooperative, measurements became increasingly difficult, and hence the decision to discontinue measuring and use unpaired measurements in the few cited cases.

The maximum allowable differences for acceptable precision used in the study for the various anthropometric variables were based on the TEM obtained in the initial standardization session conducted at the Brazilian site. To achieve a rate of remeasurement of around 5%, the maximum allowed differences were set at 2.8 times the TEM achieved during the session, i.e., 7 mm for length, 5 mm for circumferences, and 1.2 mm for skinfolds (table 2). The maximum allowable difference for weight was set at 100 g to allow for rounding off within the smallest calibration unit of the scale. Because skinfold thicknesses were the measurements with which mothers and children were least familiar and felt most uncomfortable, the decision was taken to raise the maximum allowable difference for skinfolds to 2 mm. This was considered to be a more appropriate limit, as a narrower margin might lead to too many repeat measurements, with negative implications for the anthropometrists' morale and the participants' responsiveness.

### Measurement schedule

The MGRS anthropometric measurements are weight, recumbent length, standing height, head and arm circumferences, and triceps and subscapular skinfold thickness. For the longitudinal study, newborns were measured at birth (usually within the first 12 hours of life, and never after 24 hours) and visited at home 21 times: at weeks 1, 2, 4, and 6; monthly from 2 to 12 months; and every other month during the second year (table 3). Data collection was more frequent at younger ages so that these early phases of rapid growth could be adequately described. The week 1 visit was done by the lactation counselor, and only weight was measured, following the standard MGRS procedure (using the Uniscalc and weighing the baby twice). The mother's weight was recorded at each visit, and the father's weight and both parents' heights were measured once.

In the cross-sectional study, children aged 18 to 71 months were measured once, except in the two sites that used a mixed-longitudinal design [1], in which some children were measured two or three times, at 3-month intervals. All children aged 18 to 30 months had both recumbent length and standing height measured, and parental weights and heights were measured once.

Concerted efforts were made to collect the anthropometric data on scheduled visit dates. Theoretically, the maximum delay or advance of measurements allowed by the protocol was 10% of the child's age (e.g., 3 days at 1 month, 18 days at 6 months), but in practice, teams worked with more restricted tolerable delay or advance targets (0, 1, 2, 4, and 5 days for visits at weeks 1, 2, 4, and 6 and at 2 months, respectively; 7 days for visits taking place at 3 months onwards). Of more than 32,000 home visits completed by April 2003, only 217 (0.7%) were done outside the maximum allowable delay, out of these, 58 (26.7%) exceeded the limit by less than one day.

### Measurement techniques

A comprehensive description of the techniques used for the measurements is found in the MGRS Measurement and Standardization Protocols and documented in the anthropometric training video (available on request from the first author). The anthropometrists explained to the mothers all procedures to be undertaken and emphasized that these were harmless. Infants and young children were held by their mothers to foster a sense of

TABLE 2. Maximum allowable differences between the measurements of two observers

Measurement	Brazil TEM <sup>a</sup> from pilot study	Maximum allowable difference
Weight	Not available	100 g
Length	2.5	7.0 mm
Head circumference	1.4	5.0 mm
Arm circumference	1.8	5.0 mm
Triceps skinfold	0.44	2.0 mm
Subscapular skinfold	0.43	2.0 mm

a. TEM, Technical error of measurement (see formula in footnote to table 1).

TABLE 3. Time schedule for the collection of anthropometric measurements in the longitudinal study

Measurement and time frame	Frequency	No. of visits
Weight, <sup>a</sup> length, head circumference		
Birth	Once	1
2–6 wk	Every 2 wk	4
2–12 mo	Monthly	10
14–24 mo	Every 2 mo	6
Arm circumference, skinfold thickness (triceps, subscapular)		
3–12 mo	Monthly	10
14–24 mo	Every 2 mo	6

a. Weight was also measured at week 1 by the lactation counselor.

security for the baby. The anthropometrist's confidence and poise was important for reassuring both mother and child, and included maintaining eye contact and talking to the child in a calm, reassuring voice.

Arm circumference and skinfold measurements were taken on the left side of the body. The choice of which side to measure (right or left) matters little to accuracy and precision [6]; however, the left-hand side is used more often. Length, height, circumferences, and skinfolds were recorded to the last completed unit rather than the nearest unit. To correct for the systematic negative bias introduced by this practice, half of the smallest measurement unit (i.e., half of 0.2 mm for skinfolds and half of 0.1 mm for circumferences) was added to each measurement before analysis. This correction did not apply to weight, which was rounded off to the nearest 100 g.

For measurement of weight, the mother removed all the child's clothes, but as noted earlier, use of a blanket to cover the baby was encouraged in cold weather. The parents took off their shoes, heavy clothing, and other heavy objects before being weighed. They wore light clothing of known weight that was recorded and later subtracted from the subject's weight. This was done by using a list of weights of local clothes. In the longitudinal study, the mother was weighed first, and after her weight was recorded, the scale was tared and the baby was given to her. She was asked to stand still until the baby's weight had been displayed and recorded. When children could not be undressed, they also wore standard light clothing of known weight that was recorded and subtracted to obtain the child's weight. Children aged two years or more in the cross-sectional study were weighed on their own, standing with their feet slightly apart in the center of the platform of the scale.

To measure recumbent length, braids were undone and hair ornaments were removed if they interfered with positioning of the head. Diapers were also removed, because they made it difficult to hold the infant's legs together and straighten them. The leading observer stood on one side of the board to hold down the baby's legs with one hand and move the foot board with the other. The assisting observer stood at the headboard to help position the child's head. The head was positioned so that the crown touched the headboard and a vertical line from the ear canal to the lower border of the eye socket was perpendicular to the horizontal board (i.e., the Frankfort plane positioned vertically). The leading observer positioned the child's shoulders and hips at right angles to the long axis of the body. Gentle pressure was applied to the knees to straighten the legs. To avoid causing injury, minimal but prolonged pressure was applied to the knees of newborns. To take the measurement, the footboard was positioned against the child's feet with the soles flat on the board and the toes pointing upwards. The measurement was recorded to the last completed 1 mm.

To measure standing height, hair ornaments were removed and braids were undone. The child stood on the stadiometer with bare feet placed slightly apart and the back of the head, shoulder blades, buttocks, calves, and heels touching the vertical board. The assisting observer held the child's knees and ankles to keep the legs straight and the feet flat. The leading observer got down to a face-to-face level with the child and positioned the child's head so that a horizontal line drawn from the ear canal to the lower edge of the eye socket ran parallel to the baseboard (i.e., the Frankfort plane positioned horizontally). Because young children have difficulty standing to full stature, a gentle push applied to the tummy was used to help them stand to full height. The headboard was pulled down to rest firmly on top of the head and compress the hair, and the reading was taken to the last completed 1 mm.

To measure head circumference, hairpins or headbands were removed and braids were undone. An infant or child below the age of two years was held on the mother's lap, and older children could stand or sit unassisted. The leading observer stood or sat at the left side of the child, passed the tape around the head, and anchored it just above the eyebrows and over the fullest protuberance of the skull at the back of the head. The assisting observer stood or sat in front of the child and helped by positioning the tape correctly on the side away from the lead observer. Once positioned correctly, the tape was pulled tight to compress the hair and skin, and the reading was recorded to the last completed 1 mm.

The mid-upper-arm point is half the distance between the acromion process (the most lateral bony protuberance of the back of the shoulder) and the olecranon (the bony structure that stands out when the elbow is bent). The midpoint was located and marked for measurement of the mid-upper-arm circumference (MUAC) and triceps skinfold thickness. One observer palpated the shoulder to find the acromion and marked it with a felt-tip pen or cosmetic pencil. The child's forearm was then bent 90° at the elbow, palm facing up, so that the olecranon stood out at the elbow. The observer placed the zero point of the tape on the mark over the acromion process and ran it downward along the back of the arm to the tip of the elbow. The other observer made a small horizontal mark at the midpoint on the posterior aspect of the arm before the tape was removed.

For measurement of the MUAC, the child's arm hung in a relaxed position or was held in the extended position by the assisting observer; care was taken not to flex or tighten the muscles. The tape was then wrapped around the arm over the marked midpoint. The tape had to lie flat around the arm, without compressing the skin or underlying tissue; the assisting observer checked to ensure that there was no gap or compression on the inner part of the arm before the measurement was



recorded to the last completed 1 mm.

A skinfold consists of a double fold of skin and subcutaneous fat, excluding the underlying muscle. The teams were trained to grasp the skinfold gently to avoid causing unnecessary discomfort to the child and compressing the fat. Skinfolds were recorded to the last completed 0.2 mm. For measurement of triceps skinfold thickness, young babies were held by their mothers; older children sat or stood on their own. The left arm hung relaxed at the side or was held down by the mother or assisting observer. The leading observer stood behind the child and picked up the skinfold about 1 cm above the midpoint mark over the triceps muscle, with the fold running downward along the midline of the back upper arm. The caliper jaws were applied at right angles to the “neck” of the fold just below the finger and thumb over the midpoint mark. While maintaining a grip on the skinfold, the observer gently released the caliper handles and allowed the jaws to close on the fat fold for two seconds before taking the reading to the last completed 0.2 mm.

The measurement point for the subscapular skinfold located immediately below the inferior angle of the scapula was identified by palpating and marking the inferior angle of the scapula. The child stood or sat with shoulders relaxed or gently held down to prevent movement of the scapula. The skinfold was picked up 1 cm above and medial to the subscapular mark, and the caliper was applied to the “neck” of the fold over the mark so that the fold ran diagonally down toward the left elbow. The same procedure as described for the triceps skinfold was followed to read and record the measurement.

**Quality control during data collection**

The observers’ performance was monitored in several ways during the study:

The requirement to take and record all measure-

ments independently by the two observers and to compare their measurement values for maximum allowable differences was a key strategy for detecting errors and remeasuring the child on the spot.

The proportion of repeated measurements at each site was closely monitored as an important quality control measure. Low levels of remeasurement signal a possible lack of independence between the observers, whereas high levels might indicate poor measurement techniques on the part of at least one of the observers. The levels of maximum allowable differences selected anticipated repeat rates of about 5%. The observed rates according to site are reported for newborns (fig. 2), young children in the longitudinal study (fig. 3), and older children in the cross-sectional study (fig. 4). For the overall study, the rate of repeated length measurements in the cross-sectional sample was 5%, as expected, but it was double this percentage in the longitudinal study (11%)(table 4). The lowest proportions of repeat measurements were observed for the skinfolds (3% for triceps and 1% for subscapular

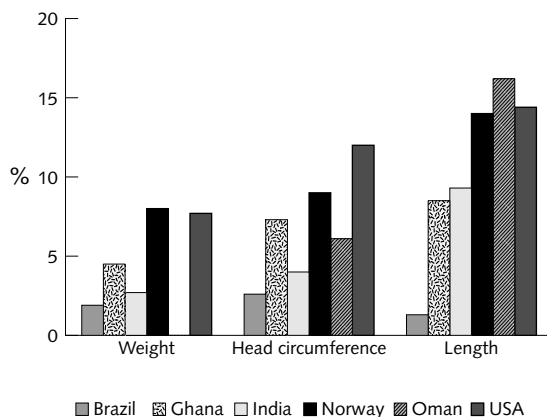


FIG. 2. Percentage of newborn measurements repeated for exceeding the maximum allowable difference between observers

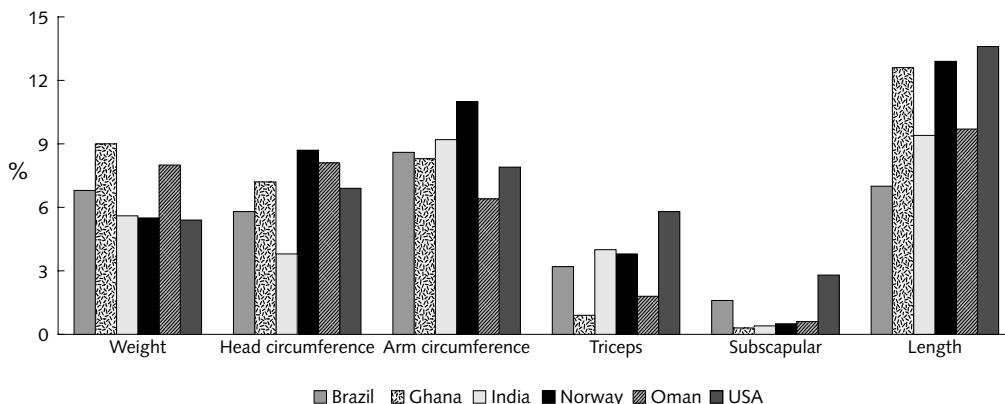


FIG. 3. Percentage of longitudinal follow-up measurements repeated for exceeding the maximum allowable difference between observers

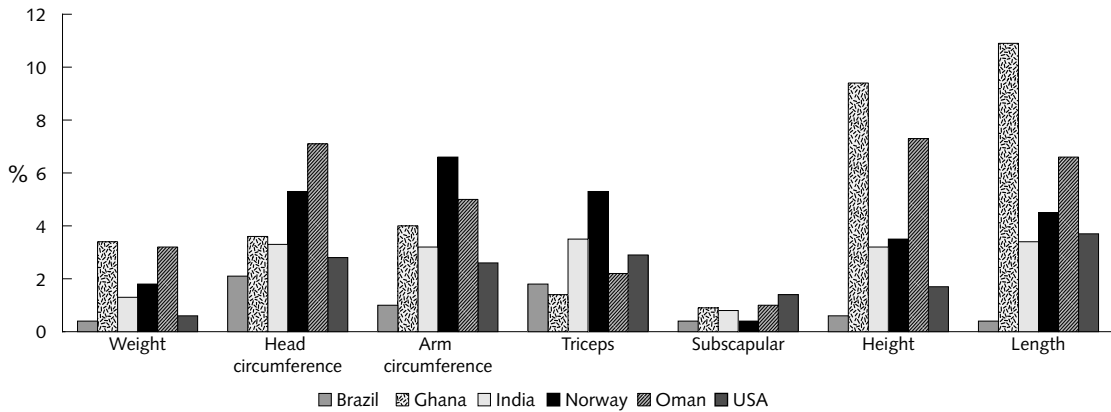


FIG. 4. Percentage of cross-sectional study measurements repeated for exceeding the maximum allowable difference between observers

TABLE 4. Summary of measurements repeated for exceeding the maximum allowable difference between observers

Measurement	No. (%) of measurements		
	Newborns ( <i>n</i> = 1,746)	Longitudinal study ( <i>n</i> = 31,248)	Cross-sectional study ( <i>n</i> = 8,254)
Weight	69 (4.0)	2,194 (6.8)	148 (1.8)
Length	180 (10.8)	3,450 (10.7)	81 (4.9) <sup>a</sup>
Head circumference	114 (6.5)	2,173 (6.8)	335 (4.1)
Arm circumference	N/A <sup>b</sup>	2,761 (8.6)	309 (3.7)
Triceps skinfold	N/A	982 (3.1)	236 (2.9)
Subscapular skinfold	N/A	300 (0.9)	69 (0.8)
Height	N/A	N/A	354 (4.3)

a. *n* = 1,653: only children aged 18–30 months in the cross-sectional study were measured for length.

b. N/A, Indices not measured.

skinfolds in both longitudinal and cross-sectional components), probably as a result of the adoption of a wider margin of allowable differences than the initial standard set in Brazil (table 4).

The completed questionnaires were delivered soon after the home visit, usually within one or two days, to the local coordination center, where they were checked by the supervisor for completeness and consistency using procedures described elsewhere in this supplement [16]. For anthropometry, the data entry system included built-in range and consistency checks that flagged measurements exceeding  $\pm 2$  standard deviations of age- and sex-specific reference values for attained size. Flagged values were then checked for consistency between the two observers, consistency with other anthropometric variables measured on the same visit, consistency with previous measurements of the same child, and possible data entry errors.

Periodic computer checks were also done for each observer to detect digit preferences and unusual values. For example, because the skinfold caliper reads to 0.2-mm units, there should be no odd decimal values (e.g., 0.1 mm, 0.3 mm) recorded for skinfolds. Table 5 is a

sample digit preference table for triceps skinfold measurements taken by one site team. The output from this analysis was examined for terminal digit preference and avoidance. According to table 5, observer 1 tended to avoid digit 6, but there was no pattern to suggest bias in observed proportions of the other digits. On the other hand, for observer 2, the proportions of digit 0 (8.4%) versus 2 (34.4%) suggested a tendency to overestimate measurements. When the imbalance between two consecutive digits was particularly large, the differences between measurement pairs were analyzed to determine whether the affected observer was biased in relation to others that had been paired with him or her.

Quality control checks were performed by randomly calling approximately 10% of the mothers to repeat a selection of the questions on the study forms and to ask the mother whether the child had been measured twice by the interviewers. These calls also provided the opportunity to monitor participant responsiveness and satisfaction with the study.

Bimonthly (every two months) standardization sessions served to ensure that the observers were not departing from the measuring techniques of the study,

TABLE 5. Sample table of terminal digit preference analysis in longitudinal follow-up study (triceps skinfold data from Oman)

Observer	No. of measurements	Terminal digit % (95% confidence interval)					Probability of equal proportions
		0	2	4	6	8	
1	773	22.6 (19.7, 25.6)	21.6 (18.7, 24.5)	20.6 (17.7, 23.4)	14.2 (11.8, 16.7)	21.0 (18.1, 23.8)	0.002
2	1,051	8.4 (6.7, 10.0)	34.4 (31.6, 37.3)	20.9 (18.5, 23.4)	16.8 (14.6, 19.1)	19.4 (17.0, 21.8)	< 0.0001
3	866	19.7 (17.1, 22.4)	25.1 (22.2, 27.9)	22.4 (19.6, 25.2)	6.6 (4.9, 8.2)	26.2 (23.3, 29.1)	< 0.0001
4	996	23.0 (20.4, 25.6)	20.2 (17.7, 22.7)	23.7 (21.1, 26.3)	15.5 (13.2, 17.7)	17.7 (15.3, 20.0)	< 0.0001
5	839	16.5 (13.9, 19.0)	20.5 (17.8, 23.2)	22.2 (19.4, 25.0)	19.2 (16.5, 21.9)	21.7 (18.9, 24.5)	0.065
6	702	16.1 (13.4, 18.8)	20.2 (17.3, 23.2)	18.0 (15.1, 20.8)	21.9 (18.9, 25.0)	23.8 (20.6, 26.9)	0.01
7	1,123	13.7 (11.7, 15.7)	23.2 (20.7, 25.6)	26.0 (23.4, 28.6)	14.0 (12.0, 16.0)	23.2 (20.7, 25.6)	< 0.0001
8	785	29.9 (26.7, 33.1)	18.6 (15.9, 21.3)	18.5 (15.8, 21.2)	15.8 (13.2, 18.4)	17.2 (14.6, 19.8)	< 0.0001
9	657	19.8 (16.7, 22.8)	20.1 (17.0, 23.2)	21.2 (18.0, 24.3)	16.4 (13.6, 19.3)	22.5 (19.3, 25.7)	0.1514

to monitor precision and accuracy, and to take corrective measures (e.g., retraining) when required.

To maintain a good rapport with the families, each participant in the longitudinal study had one "fixed" fieldworker for the duration of the follow-up. The other fieldworkers were rotated every two months in order to distribute error terms, avoid boredom, and prevent complicity that might undermine the measurement protocol.

## Discussion

The rigorous anthropometric protocols described in this paper were set in place to ensure high data quality. These MGRS procedures serve as a model for research settings. The methods and procedures reviewed will be applicable to multi- and single-site studies. It will not be possible to be as rigorous in nonresearch settings, such as child clinics. At the very least, the procedures should be carefully documented in training manuals, staff members collecting anthropometric data should be trained and refresher sessions should be held periodically, weighing scales and any other instruments used should be maintained in good order and calibrated before use, and fieldworkers should be supervised.

The standardization sessions were effective in identifying factors that contribute to low accuracy and precision in anthropometric measurements. Training and retraining opportunities were available to help keep the anthropometrists' skills sharp, as were printed and videotaped reference materials. These were particularly useful when reserve staff were preparing to take part

in data collection and when new team members were recruited in the course of the study. In general, new staff began taking anthropometric measurements for the MGRS only after being standardized against the WHO lead anthropometrist.

Factors that affected measurement accuracy and precision included the identification of landmark features when measuring soft tissues (arm circumference and skinfolds). In some sites, the teams experienced difficulties in taking measurements because they did not mark the upper-arm midpoint or the subscapular point. In this respect, the Coordinating Centre's ongoing monitoring of anthropometric data and the regular participation of the WHO lead anthropometrists in site standardization sessions were extremely important for detecting and correcting problems.

For research and programmatic activities, it is relevant to note that the child's age could affect the precision of some measurements, judging by the differences in repeat rates for arm circumference (9% versus 4%) and head circumference (7% versus 4%) in the longitudinal and cross-sectional studies, respectively. Users who adopt the same limits of maximum allowable differences between independently recorded duplicate measurements could evaluate performance with the MGRS-observed proportions as a reference. Thus, for children below the age of two years, about 11% of length measurement pairs will differ by more than 7 mm. In the same age group, 7% of duplicate head circumferences will differ by more than 5 mm, as will 9% of duplicate arm circumference measurements. Overall, the rates of repeated measurement are expected to be lower in older children, who tend to be

calmer and more cooperative. A team that exceeds these proportions may be in need of further training, and a

team that has substantially lower rates may be taking nonindependent measurements.

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# Assessment of gross motor development in the WHO Multicentre Growth Reference Study

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## Abstract

*The objective of the Motor Development Study was to describe the acquisition of selected gross motor milestones among affluent children growing up in different cultural settings. This study was conducted in Ghana, India, Norway, Oman, and the United States as part of the longitudinal component of the World Health Organization (WHO) Multicentre Growth Reference Study (MGRS). Infants were followed from the age of four months until they could walk independently. Six milestones that are fundamental to acquiring self-sufficient erect locomotion and are simple to evaluate were assessed: sitting without support, hands-and-knees crawling, standing with assistance, walking with assistance, standing alone, and walking alone. The information was collected by both the children's caregivers and trained MGRS fieldworkers. The caregivers assessed and recorded the dates when the milestones were achieved for the first time according to established criteria. Using standardized procedures, the fieldworkers independently assessed the motor performance of the children and checked parental recording at home visits. To ensure standardized data collection, the*

*sites conducted regular standardization sessions. Data collection and data quality control took place simultaneously. Data verification and cleaning were performed until all queries had been satisfactorily resolved.*

**Key words:** Child, child development, infant, longitudinal study, motor development, motor skills

## Introduction

Motor behavior is an essential aspect of child development. Given the unique opportunity provided by the World Health Organization (WHO) Multicentre Growth Reference Study (MGRS), a component to assess gross motor development was included in the protocol. Motor development is usually assessed in terms of age of achievement of motor milestones [1]. Besides the determination of age at attainment, longitudinal assessment of different types of motor skills has the advantage of providing a profile of their sequence and tempo [2, 3]. However, few studies using a longitudinal design have been done on the age of achievement of certain motor milestones [4–21], and only two of them are of a multicountry nature [10, 21].

To our knowledge, this is the first longitudinal study that has used a standardized protocol to describe gross motor development among groups of children with no health, environmental, or economic constraints on growth, living in different countries. The study sample described by the WHO Task Force for Epidemiological Research on Reproductive Health [21] was stratified into three different socioeconomic-level groups, and the study of Hindley et al. [10] was limited to the assessment of one motor milestone. The MGRS aimed to fill this gap in information by collecting data on six gross motor milestones in five of the countries participating in its longitudinal growth and development study: Ghana, India, Norway, Oman, and the United States. Under the umbrella of the MGRS, the Motor Develop-

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

ment Study provides a unique opportunity to assess group and individual variability in the acquisition of key motor skills, as well as providing an opportunity to analyze the relationship between physical growth and gross motor development among groups of affluent children growing up in different cultural settings.

This paper outlines the Motor Development Study protocol for collecting information on six motor milestones, the methods and procedures of data collection, and the training and standardization of fieldworkers.

## Methods

### Study subjects and study design

The motor development assessments were done from the age of four months on all subjects enrolled in the longitudinal component of the MGRS. Details of the enrollment of subjects, the inclusion criteria, and the MGRS study design are explained elsewhere in this supplement [22]. The study took place in five of the six countries participating in the MGRS: Ghana, India, Norway, Oman, and the United States. The implementation of the study protocols in each of these countries is described in separate papers in this supplement [23–27]. The Brazilian site was unable to participate in the Motor Development Study because the site had initiated data collection by the time the decision to assess motor development was taken.

### Gross motor milestones: description, criteria, and testing procedure

Six distinct gross motor milestones were selected for study: sitting without support, hands-and-knees crawling, standing with assistance, walking with assistance, standing alone, and walking alone. These milestones were selected because they are considered to be universal, fundamental to the acquisition of self-sufficient erect locomotion, and simple to test and evaluate.

Before the achievement of any of the six motor skills, the child goes through many preceding intermediate stages of development [28, 29]. Evaluation of a milestone performance consists in observing not only what a child does, but also how and with what level of development he or she does it [29]. There is also a need to include in the criteria for testing whether a child can perform a milestone independently or performs it after having been placed into position [30]. Thus, in order to minimize interpersonal interpretation differences, each test item needed to be clearly defined with respect to the method of administration and the interpretation of the child's performance [1].

The descriptions of the six gross motor skills used in this study originated from various existing developmental scales [2, 29, 31–35]. The sequential presentation of the motor milestones followed the pattern generally found in the literature [36–40]. However, occasionally the suggested sequence between two or more milestones might actually be reversed, and observed milestones might be inhibited later [28]. Therefore, no fixed developmental sequence of achievement was assumed.

All milestones were assessed using standardized

TABLE 1. MGRS performance criteria for six gross motor milestones

Gross motor milestone	MGRS performance criteria
Sitting without support	Child sits up straight with the head erect for at least 10 seconds. Child does not use arms or hands to balance body or support position
Hands-and-knees crawling	Child alternately moves forward or backward on hands and knees. The stomach does not touch the supporting surface. There are continuous and consecutive movements, at least three in a row
Standing with assistance	Child stands in upright position on both feet, holding onto a stable object (e.g., furniture) with both hands without leaning on it. The body does not touch the stable object, and the legs support most of the body weight. Child thus stands with assistance for at least 10 seconds
Walking with assistance	Child is in upright position with the back straight. Child makes sideways or forward steps by holding onto a stable object (e.g., furniture) with one or both hands. One leg moves forward while the other supports part of the body weight. Child takes at least five steps in this manner
Standing alone	Child stands in upright position on both feet (not on the toes) with the back straight. The legs support 100% of the child's weight. There is no contact with a person or object. Child stands alone for at least 10 seconds
Walking alone	Child takes at least five steps independently in upright position with the back straight. One leg moves forward while the other supports most of the body weight. There is no contact with a person or object

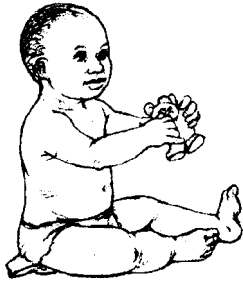


FIG. 1. Sitting without support

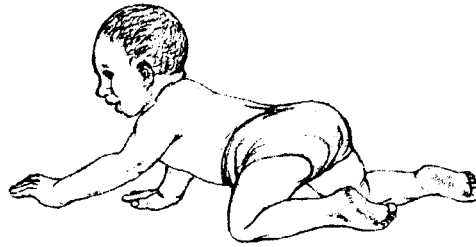


FIG. 2. Hands-and-knees crawling

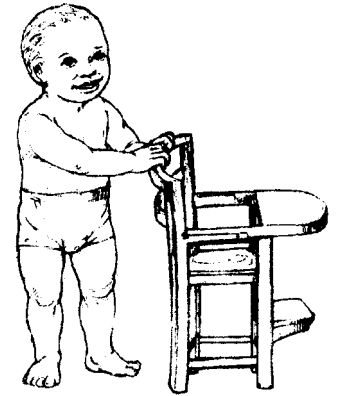


FIG. 3. Standing with assistance

testing procedures. Table 1 describes the MGRS performance criteria for the six milestones. A milestone was considered achieved only if all the given criteria were met.

#### **Sitting without support (fig. 1)**

*Description.* The child is able to balance the weight of the trunk and head without any external support or the use of arms and hands. The child sits up straight with the head erect (that is, not leaning forward). One of the lower limbs is usually flexed.

*Criteria.* (a) The child's head is erect; (b) the child does not use the arms or hands to balance body or support position; (c) the child sits up straight for at least 10 seconds.

*Testing procedure.* Facing the child and smiling, the fieldworker places the child in a sitting position. The fieldworker then gives the child a toy to handle with both hands so that he or she is not able to use the arms to support himself or herself.

#### **Hands-and-knees crawling (fig. 2)**

*Description.* This is a phase of a more organized prone movement that refers to the palm-knee position, with alternating movements of the upper and lower limbs: the right arm and left leg move forward or backward synchronously and vice versa in similarly ordered consecutive movements.

*Criteria.* (a) Alternating movement forward or backward on hands and knees; (b) the child's stomach does not touch the supporting surface; (c) continuous and consecutive movements, at least three in a row.

*Testing procedure.* The fieldworker places the child in the prone position with the abdomen above the supporting surface. The fieldworker places himself or herself in front of the child, about 120 to 150 cm away. If the child does not crawl spontaneously, the fieldworker shows the child a toy or object that attracts the child's visual attention. The fieldworker (sometimes with the help of the caregiver) then tries to coax the child to crawl toward the toy and grab it.

#### **Standing with assistance (fig. 3)**

*Description.* This is the first direct step toward erect bipedal locomotion, in which the child is for the first time challenged to maintain some balance of the whole body weight so that he or she can move forward. The salient characteristic is whether the child can actually support his or her weight if he or she is holding onto a stable object (e.g., a piece of furniture) with both hands without leaning over or resting the body on the stable object.

*Criteria.* (a) The child is in an upright position on both feet; (b) the child holds onto a stable object with both hands without leaning on it; (c) the child's body does not touch the stable object; (d) the child's legs support most of the child's body weight; (e) the child thus stands with assistance for at least 10 seconds.

*Testing procedure.* The fieldworker places the child in a standing position so that the legs support the body weight. The child is placed at a distance from which both hands, but not the body, can reach and hold onto a stable object. Thus, most of the body weight is supported by the child's own feet. The fieldworker should check that the child is not leaning over or resting his or her body on the stable object. The height of the stable object should be at about the same level as the child's stomach.

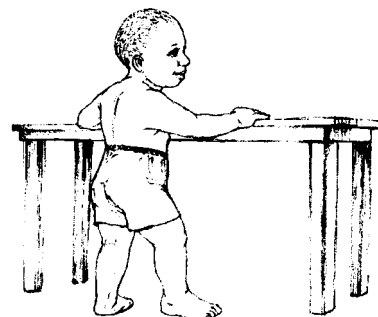


FIG. 4. Walking with assistance

### Walking with assistance (fig. 4)

*Description.* This involves a deliberate attempt to make stepping movements and to make postural adjustments toward this end while holding onto a stable object (e.g., furniture) for support.

*Criteria.* (a) The child is in an upright position with the back straight; (b) the child makes sideways or forward steps by holding onto a stable object with one or both hands; (c) one leg moves forward while the other supports part of the body weight; (d) the child takes at least five steps in this manner.

*Testing procedure.* The fieldworker places the child in a standing position so that the legs support most of the body weight. The child is placed at a distance from which he or she can reach and hold onto a stable object with one or both hands. If the child does not move spontaneously, the fieldworker shows the child a toy or object that attracts the child's visual attention. The fieldworker (sometimes with the help of the caregiver) then tries to coax the child to walk toward the toy and grab it. The height of the stable object should be at about the same level as the child's stomach.

### Standing alone (fig. 5)

*Description.* The child shows the capacity for both equilibration and sustaining body weight on the feet. In this position the child's legs show no flexion, and the child is standing on the feet (not on the toes) without leaning over or holding onto an object. The child maintains continuous balance independently.

*Criteria.* (a) The child is in an upright position on both feet (not on the toes) with the back straight; (b) the child's legs support 100% of the child's weight; (c) there is no contact with a person or an object; (d) the child stands alone for at least 10 seconds.

*Testing procedure.* The fieldworker places the child with both feet flat on the floor and supports the child to an erect position. Then the fieldworker withdraws the support gradually and temporarily to determine

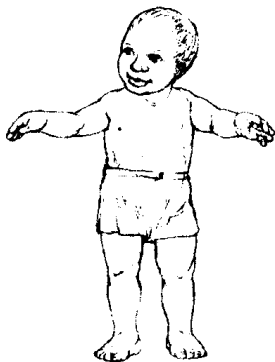


FIG. 5. Standing alone

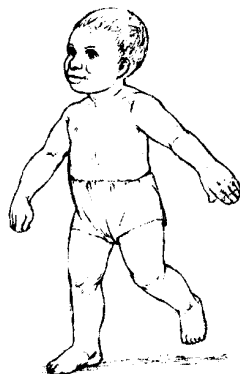


FIG. 6. Walking alone

whether the child can modify posture, adjust to the new position, and stand alone for at least 10 seconds.

### Walking alone (fig. 6)

*Description.* The child shows the capacity to balance the body and to control his or her forward stepping movements. There is no need for assistance, because both the postural adjustment and the stepping movements are engaged in independent walking. An important indicator of this phase of erect locomotion is that movement of the entire body does not accompany the child's stepping movements. This phase does not refer to the child's first independent steps when the child is able to take three or four uncertain steps toward the adult's outstretched hands.

*Criteria.* (a) The child is in an upright position with the back straight; (b) one leg moves forward while the other supports most of the body weight; (c) there is no contact with a person or an object; (d) the child takes at least five steps independently.

*Testing procedure.* The fieldworker places the child in an erect position out of the reach of any supporting object. Then the fieldworker takes a position about 120 to 150 cm in front of the child and calls the child to move toward the fieldworker. Sometimes, the caregiver needs to encourage the child.

### The child's emotional state

Because emotional arousal can either enhance or undermine motor behavior, the fieldworker rated the overall emotional state of the child during the testing of all the six gross motor milestones according to two scales [41]. First, the scale of consciousness was rated either as drowsy or as awake and alert. Second, the child's irritability was rated as being calm, fussy, or upset (crying).

Ideally, the child should be awake, alert, and calm during the assessments of motor skills. Drowsiness, fussiness, and crying were not reasons for not testing if the child was still able to display the milestone under testing. However, if they interfered with assessment, the child was retested when he or she was calm. If a child was asleep, he or she was not woken up to be tested.

In the context of the MGRS, the fieldworkers preferably tested the child on the motor skills after the completion of the anthropometric measurements. However, if the child was known to become upset by the anthropometric measurements, testing on motor milestones occurred prior to these measurements. If the caregiver and/or the child were obviously distraught or if the child was sick during a follow-up visit, testing did not occur.



## Training and standardization of fieldworkers

### Training

The MGRS fieldworkers selected to carry out the motor development assessments were trained at their own study site by an external expert prior to the initiation of data collection. The training involved lectures, discussions, observations, and assessments of a group of about 30 children (aged 5–13 months). It consisted of two days of initial training, one day of evaluation of the trainees, and two days of guided home visits. During the two-day initial training, the assessments carried out by the trainees were videotaped and reviewed afterwards by the trainer and trainees. The evaluation session (which was recorded as well) assessed the trainees' ability to score the achievement of the six motor milestones. This session involved both trainer and trainees. The trainer tested and scored approximately 10 to 15 children (aged 5–13 months) and did not give any indication of the children's scores to the caregivers or trainees. The trainees observed the child being tested and independently scored the child's performance on each tested skill. After the evaluation, the trainees' scores were compared with the trainer's scores, and in case of disagreements, these were discussed by looking at the videotaped session.

### Standardization

The sites conducted regular half-day standardization sessions to determine the interobserver reliability rates of fieldworkers. During each session, one member of the fieldworkers' team tested and scored a group of about 10 children (aged 6–12 months) for the six motor milestones. The assessment and performance of the children were videotaped for subsequent scoring by the other fieldworkers at the same site. At each session, the fieldworker doing the actual testing was rotated so that a different person was the tester. The child's caregiver was present but was requested not to interfere with the assessments. However, when needed, the tester asked for the caregiver's assistance. The tester did not give any indication of the child's scores and wrote them on a standardization record form. Milestone performance could be rated as inability, refusal, ability, or unable to test, according to the established criteria (see below). The other fieldworkers watched the videotaped session and independently scored the performance of the same children on each of the six milestones.

After the conduct of each session, the videotape of the session and the fieldworkers' scores were sent to the Coordinating Centre of the MGRS at WHO in Geneva. The Motor Development Study coordinator on the Coordinating Centre team viewed the tape and scored the performance of the children. The scores given by the coordinator were considered to be the standard (true) scores. Interobserver reliability rates (percent-

ages of agreement) were generated by calculating a correlation between the standard score and the scores obtained by the tester and the observers in a site.

The results of the sessions and comments on the observed disagreement between the standard score and a fieldworker's score, as well as on the tester's performance of the assessments, were sent as feedback to the site. A cutoff point of 90% agreement was set to determine whether further training was required.

### Standardization of conditions for testing

It is well documented that child rearing practices [42] and encouragement by training and practice [28, 43] account for part of the variability in the achievement of motor milestones. Data collection in the study took place at the children's homes so that the standardization of the environment was limited. One source of variability, however, that could be controlled for was the social and physical context in which the child was tested and the nature of the objects used for testing. If physically possible and culturally appropriate, the number of persons present during testing was limited to three (fieldworker, caregiver, and child). If limitation of the number of people in the room was not possible, it was imperative that other observers did not move or make verbal comments during testing unless requested. Ideally, the surface of the floor where the assessments took place was clean and free of objects that might interfere with locomotion. Prior to testing, the fieldworker asked the caregiver to select a maximum of three toys or objects that the child liked to play with. It was primarily the fieldworker who carried out motor development assessment during the home visits. However, in some cases it was necessary for the fieldworker to ask for the caregiver's help.

### Data collection

The data were recorded by the child's caregivers between follow-up visits and by the trained follow-up team members during these scheduled visits to the children's homes.

### Caregiver

At the four-month follow-up visit, the caregiver was informed about the Motor Development Study and asked to start observing and assessing the child's motor developmental level until the child had achieved all six milestones. The caregiver was told to place the child in the appropriate position according to the defined testing procedures as soon as the caregiver observed that the child was making the first movements toward the achievement of a particular milestone. No fixed order of milestone achievement was assumed.

The record form for the caregiver had one page and presented the six drawings of the milestones (figs.

1–6), along with the performance criteria. A date box for each milestone was given, in which the caregiver recorded the date the child met the criteria for this item and thus achieved it for the first time. As soon as the caregiver had recorded the dates of first appearance of all six milestones, the caregiver stopped the motor development assessments.

#### **Fieldworker**

The follow-up team member trained in motor development assessments tested and scored all of the six gross motor milestones at each home visit. When both fieldworkers doing the home visits had been trained in motor development assessment, only one of them carried out the assessment and scored the child without the involvement of the other fieldworker. It was not necessary that the same fieldworker carry out all the motor development assessments for a given child. Motor development assessments were carried out monthly during the first year of life, starting from the five-month visit, and then every two months in the second year of life until the child acquired the skill of independent walking. If at the four-month visit, the time point when the fieldworker informed the caregiver about the study, the fieldworker observed that a child had achieved a certain milestone or a caregiver reported its achievement, then the fieldworker started the assessment at that visit. The reasons for examining all the milestones at each home visit were standardization of data collection across study sites, the fact that motor milestones might not occur in a sequential way in all subjects, and the fact that some milestones might be observed and then inhibited later (e.g., after an illness or trauma).

The performance of each milestone was evaluated independently by using four coding possibilities: inability—the child tried but failed to perform the test item because it surpassed his or her developmental level; refusal—the child was calm and alert but just refused to cooperate; ability—the child performed the test item according to the specified criteria; and unable to test—the child could not be tested on this milestone because his or her emotional state (drowsiness, fussiness, or crying) was interfering with testing, the child was sick, or the child's caregiver was distraught. In practice, it was somewhat difficult to differentiate between “refusal” and “unable to test.”

The fieldworker took about 10 minutes to test all milestones. Since it was not always possible to get the child's cooperation immediately, the fieldworker was allowed three trials for the assessment of each milestone. The fieldworkers were given no ages at which the infants were expected to achieve each milestone, as this might have influenced their judgment.

For milestones that had not been achieved by the 12-month visit, the fieldworkers called the caregivers in the months with no scheduled follow-up visit during the

second year of follow-up (i.e., months 13, 15, and 17). The fieldworker asked whether the child had achieved a specific milestone and reminded the caregiver to fill out the parent's record form. If the child had achieved a specific milestone, the fieldworker verified this by going through the criteria with the caregiver on the phone. Afterwards, at the planned home visit the following month, the fieldworker checked the acquisition of the reported milestone. Figure 7 shows the data collection form used by the fieldworkers for the motor development assessment.

#### **Parental recording**

At each visit, the fieldworker asked the caregiver about the milestones achieved since the previous follow-up visit and obtained the date that the caregiver had written down on the record form. If it was found on examination that the milestone(s) reported by the caregiver had not actually been attained by the child, the fieldworker carefully discussed this with the caregiver and explained the criteria again to make sure that the caregiver understood the criteria for the specific milestone. If the caregiver agreed that the child did not fulfill all the criteria, the fieldworker drew a new date line below the recorded date on the parent's record form for the milestone involved and asked the caregiver to record the date when this milestone was achieved according to the established criteria. If, on the other hand, the caregiver was sure that the child had met the criteria for the milestone, the fieldworker transferred to the form (fig. 7) the first written date as the caregiver's recorded date. The fieldworker also verified whether the caregiver had actually tested and recorded the date or simply recalled the date of first achievement. If a child happened to perform the motor skill for the first time at a certain home visit, this date was entered as the caregiver's date. The fieldworker never told the caregiver when a child should be achieving a particular milestone or gave any indication about which milestones the caregiver should be looking for as the child got older.

#### **Data quality control**

Data quality assurance started with the fieldworkers carefully filling out the record forms and checking for completeness and accuracy. Additional checks were made by data quality control staff and supervisors at the sites. Extensive quality checking was carried out on the data accumulated at the Coordinating Centre. A printout of the complete set of Motor Development Study records for each child was checked periodically for inconsistencies, such as missing or incorrectly entered caregiver's dates, reported caregiver's date without confirmation of a milestone's achievement by a fieldworker, discontinuation of the Motor Development Study without observed achievement of all


 WORLD HEALTH ORGANIZATION		Multicentre Growth Reference Study Project NUT01 – Motor development assessment		MDS
Identification		Test items	Examiner report	Caretaker report
(a) Form code:	MDS		(a) Observed 1 = No (inability) 2 = No (refusal) 3 = Yes 9 = Unable to test	(b) Precise date of first achievement (Taken from the parent's record form). Only enter date(s) for milestone(s) achieved for the first time between the previous follow-up and present visit.
(b) Study number:	NUT01	1. Sitting without support	<input type="checkbox"/>	<input type="checkbox"/>
(c) Site number:	<input type="checkbox"/>	2. Hands-and-knees crawling	<input type="checkbox"/>	<input type="checkbox"/>
(d) Subject code:	<input type="checkbox"/> - <input type="checkbox"/>	3. Standing with assistance	<input type="checkbox"/>	<input type="checkbox"/>
(e) Follow-up visit number:	<input type="checkbox"/>	4. Walking with assistance	<input type="checkbox"/>	<input type="checkbox"/>
(f) Continued testing required? 1 = No 2 = Yes	<input type="checkbox"/>	5. Standing alone	<input type="checkbox"/>	<input type="checkbox"/>
(g) Date of visit:	<input type="checkbox"/> / <input type="checkbox"/> / <input type="checkbox"/> Day Month Year	6. Walking alone	<input type="checkbox"/>	<input type="checkbox"/>
(h) Examiner's code:	<input type="checkbox"/>	7. Child's emotional state Rate the child's emotional state during the testing of all the milestones.  Enter a code for each of the two scales.	(a) First scale 1 = Drowsy 2 = Awake and alert	(b) Second scale 1 = Calm 2 = Fussy 3 = Crying
Remarks				

FIG. 7. Fieldworker's data collection form for motor development assessment

six milestones, or order of milestone achievement (e.g., walking alone before walking with assistance). The reported inhibition of a milestone was queried as well as differences between a Motor Development Study home visit date and a follow-up visit date. The inconsistencies were sent to the sites for investigation, verification, and correction at the source. This process of data verification and cleaning between the sites and the Coordinating Centre was continued until all data queries had been satisfactorily resolved. Detailed descriptions of the MGRS data management procedures are given elsewhere in this supplement [44].

## Conclusions

The Motor Development Study aimed to describe the acquisition of six universal gross motor milestones in the first two years of life among affluent children growing up in different cultural settings, and thereby fill an existing gap in knowledge. The uniqueness of this study includes the opportunity to link growth and motor development in one international reference. The same protocol was used in the five countries that participated in the study, and the motor development assessments were performed by standardized fieldworkers. This is expected to minimize the influence of respondent biases on the outcome. At the

same time, having caregiver records of the exact dates of milestone achievement facilitates internal cross-validation with fieldworkers' records and comparison of the MGRS data with previous studies that relied on parental reporting alone. Achievement of the six milestones was assessed repeatedly between 4 and 24 months of age, which will make it possible to describe their sequence and tempo in addition to the ages when milestones were acquired. The availability in the MGRS of information on breastfeeding and complementary feeding will also permit studies of associations between child feeding and motor development.

Although the study was conducted in a standardized manner, it also had limitations. We did not collect information on stimulation and child rearing practices that might influence milestone acquisition [28, 42, 43]. Thus, although it will be possible to examine associations between motor development and child feeding, morbidity, and overall physical growth, assessment of the possible influence of psychosocial stimulation on the reported outcomes will be limited to the examination of their ecological associations with the socioeconomic and demographic profiles found in the MGRS. Despite this limitation, this study provides an important addition to the literature on gross motor development in different cultural settings and should serve as a baseline for more focused studies of both motor and cognitive development.

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# Managing data for a multicountry longitudinal study: Experience from the WHO Multicentre Growth Reference Study

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference (MGRS) data management protocol was designed to create and manage a large data bank of information collected from multiple sites over a period of several years. Data collection and processing instruments were prepared centrally and used in a standardized fashion across sites. The data management system contained internal validation features for timely detection of data errors, and its standard operating procedures stipulated a method of master file updating and correction that maintained a clear trail for data auditing purposes. Each site was responsible for collecting, entering, verifying, and validating data, and for creating site-level master files. Data from the sites were sent to the MGRS Coordinating Centre every month for master file consolidation and more extensive quality control checking. All errors identified at the Coordinating Centre were communicated to the site for correction at source. The protocol imposed transparency on the sites' data management activities but also ensured access to technical help with operation and maintenance of the system. Through the rigorous implementation of what has been a highly demanding protocol, the MGRS has accumulated a large body of very high-quality data.*

**Key words:** Data collection, data processing, database management system, longitudinal study

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

## Introduction

The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) data management system was set up and operated according to a protocol designed to ensure a high quality of banked data, stored securely against unauthorized manipulation and accidental loss. The data were collected over a period of more than six years (July 1997 to November 2003) and in six different sites with variable levels of data management experience. In this context, using a standardized protocol in all study sites simplified the compilation and maintenance of the central master files at the MGRS Coordinating Centre as well as facilitating Coordinating Centre-to-site and intersite technical support whenever required. The system also imposed transparency to the extent that the Coordinating Centre could replicate and extend key elements of the quality control procedures that sites were expected to carry out as part of the data collection and management protocols. The confidentiality of the study participants was ensured by limiting identification information in the study data files to numbers without names or other information that might identify them beyond the purposes of the study.

The purpose of the present article is to share experience gained in managing the large body of data collected in the MGRS. We describe the data management model, the standard operating procedures (SOPs) used for handling forms and data, the computerized system with its inbuilt quality assurance features, the respective responsibilities of the sites and the Coordinating Centre, data quality checking and cleaning during the data collection phase, and the closure of data management activities in the sites.

## General organization of the data management system

The longitudinal and cross-sectional components of the MGRS are described elsewhere in this supplement

[1], where detailed information on the specific data collected from the sample is also provided. In the data management environment, the longitudinal and cross-sectional study components were treated as separate projects with respect to assembling and processing batches of data and creating master files.

Briefly, the longitudinal study data set consists of eight master files, the first of these being the file that describes all screened subjects, regardless of whether or not they were enrolled in the study. Other questionnaires recorded information on the initiation of breastfeeding in the hospital and its continuation at home; baseline demographic and parental characteristics; child feeding, morbidity, and anthropometry during follow-up; and motor development. All enrolled subjects had an end-of-participation form completed indicating when they ended participation and for what reason. The eighth longitudinal study master file contains data from the 12-month study involving refusals and early dropouts who agreed to respond to an interview on the child's first birthday. The cross-sectional data set comprises two essential files: a screening master file with records of all screened subjects, and a survey master file with records of all subjects who responded to the cross-sectional study interview and had their anthropometric measurements taken. One supplemental form was used in Brazil and the United States,

where the mixed-longitudinal design was used [1–3]. In these two sites, some cross-sectional study participants received one or two follow-up visits at which an abbreviated version of the survey questionnaire was used to collect data on anthropometry and intercurrent morbidity. A summary of the types of forms and number of records accumulated by each site up to end of May 2003 is presented in table 1 for the longitudinal study and table 2 for the cross-sectional study.

### Preparatory work and system setup

A decentralized data management model was chosen for the study: each site collected, entered, verified, and validated data, and then locally created, updated, and cleaned study master files. Copies of the data files were transferred every month to the Coordinating Centre, where the consolidated study master files were created and updated with incoming data from the sites. Figure 1 illustrates the data flow and summarizes the tasks undertaken by the sites and the Coordinating Centre.

In order for this organizational system to work, the sites followed a common data management protocol, which included the use of centrally prepared data collection forms (questionnaires) and the same data processing system (software and dictionaries). The

TABLE 1. Longitudinal study forms received by May 2003

Form	Brazil ( <i>n</i> = 4,801)	Ghana ( <i>n</i> = 2,057) <sup>a</sup>	India ( <i>n</i> = 692) <sup>a</sup>	Norway ( <i>n</i> = 836)	Oman ( <i>n</i> = 4,957)	USA ( <i>n</i> = 398)	All countries ( <i>n</i> = 13,741)
Screening	4,801	538	433	836	4,957	398	11,963
Breastfeeding (hospital)	—	343	353	322	446	237	1,701
Breastfeeding (home)	—	1,241	1,254	1,188	1,221	834	5,738
Baseline	368	351	331	308	328	212	1,898
Follow-up	5,864	6,090	5,435	5,605	5,488	3,843	32,325
12-month visit	101	12	60	41	72	28	314
Motor development	—	2,651	2,623	2,209	2,436	1,726	11,645
End of participation	388	364	234	322	450	232	1,990
All forms	11,522	11,590	10,723	10,831	15,398	7,510	67,574

*a.* Ghana and India prescreened subjects owing to local circumstances [4, 5] before the MGRS screening interview was administered, hence the difference between the number of subjects and the number of screening forms in these 2 sites.

TABLE 2. Cross-sectional study forms received by May 2003

Form	Brazil ( <i>n</i> = 2,292)	Ghana ( <i>n</i> = 4,622)	India ( <i>n</i> = 3,886)	Norway ( <i>n</i> = 5,185)	Oman ( <i>n</i> = 4,509)	USA ( <i>n</i> = 919)	All countries ( <i>n</i> = 21,413)
Screening	2,292	4,622	3,886	5,185	4,509	919	21,413
Cross-sectional survey	487	1,323	1,490	1,387	1,432	562	6,681
Follow-up survey I	450	—	—	—	—	422	872
Follow-up survey II	419	—	—	—	—	364	783
All forms	3,648	5,945	5,376	6,572	5,941	2,267	29,749

electronic dictionaries in the data management system exactly matched the questionnaires and interviewer guides. For example, the interviewer guide specified when contingency questions were to be skipped, and the data entry dictionary had a corresponding rule to skip the variable during data entry in order to reduce unnecessary key punching. To facilitate data entry further, electronic forms were formatted so that the data entry screens matched the pages of each respective data collection form. In sites where questionnaires required translation from English (Brazil, Norway, and Oman), they were translated into the local language and independently back-translated into English to ensure that the content of the questions remained unchanged. The interviewer guides were also translated in these sites.

Before the start of data collection, the data manager of each site participated in a week-long training workshop at the Coordinating Centre in Geneva. The workshop included a presentation of the WHO Good Clinical Practice and data management principles [6], and the DMS/2 data processing software for data entry, verification, validation, and file update. Exercises and dummy runs were organized to ensure that participants clearly understood the SOPs in data management and why it was important to implement them. Some time was devoted to discussing and defining the responsibilities of the sites and the Coordinating Centre with respect to data monitoring, transferring study data, and obtaining help whenever required. Before data collection began, each data manager was given a timetable

with exact dates for monthly data submission to the Coordinating Centre for the duration of the data collection phase.

The complete system installation package was distributed to each data manager. This included the full set of dictionaries for all study questionnaires and the DMS/2 software with documentation for its operation. The dictionary for each form defines its data variables and types, labels, plausible value ranges, and data entry skip-and-fill rules, as well as intervariable cross-checks. The data managers were involved in interviewer training before data collection began in the site to stress the importance of completing the questionnaire forms legibly and according to the instructions in the interviewer guides.

### Standard operating procedures at site level

The data management procedures are simple and follow a natural sequence. The data manager had to ensure that each step was successfully completed before moving to the next. Because of the repetitiveness of these operations during data collection, it is easy to miss a problem, therefore the need for rigorous application of the procedures was emphasized during training.

Each form received from interviewers was manually checked for legibility, completeness, and consistency, and any additional coding was done at this stage. All

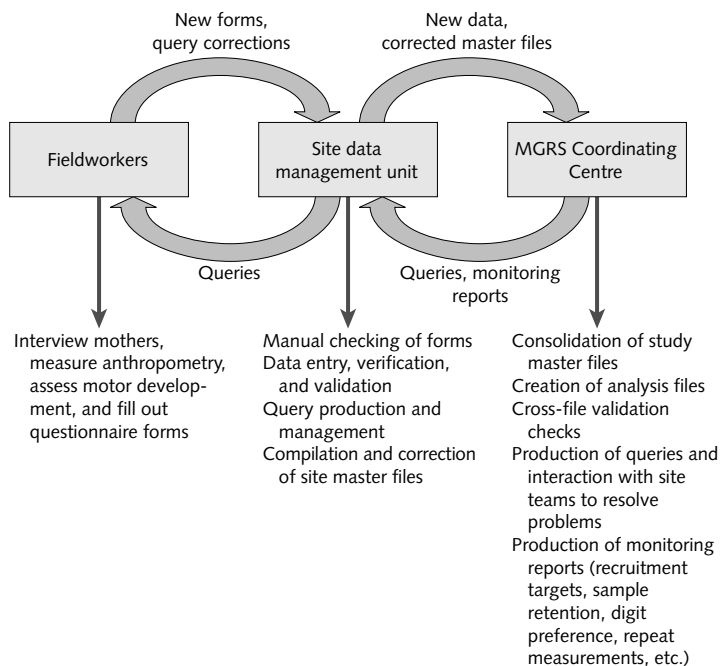


FIG. 1. Data management standard operating procedures and data flow at sites and at the Coordinating Centre



forms received were recorded in the subject form register, a manual or electronic spreadsheet that indicated completed visits and when they had been done for each subject. The subject form register facilitated timely detection and correction of duplicated forms and errors in subject identification, and helped to keep track of missed visits and losses to follow-up. The data managers periodically printed out a computer form register, a replica of the subject form register showing which forms had been accumulated in the master files for each subject. This was a useful double-checking tool for identifying any forms that might have been misplaced between reception at the study center and the data entry unit.

The forms received over one or two days were assembled into a batch that was assigned an identification number. An entry for the batch was added to the batch log register. A cover form was attached to each batch to indicate its source and contents (number and types of form and subject identification numbers). This form provided spaces for recording the dates when the batch was received, entered, verified, validated, and updated to master files. All forms in a batch remained under the same cover until they had been processed through to master file updating. With the batch cover form in order, the batch was sent for data entry. The SOPs specified that data be entered twice, preferably by different data entry operators. For the first entry, the operator activated the relevant electronic dictionaries by indicating which forms were included in the batch. The operators were trained and required to key in data exactly as they appeared on the form. The second entry was done on the same or following day. For this run, the system was set to verification mode, that is, the original entries were hidden and the operator keyed the same data over them. Whenever there was a discrepancy between the original and the verification entry, the system stopped and the operator was required to verify the correct information from the form and enter it.

The next step was to validate the data. This was done on the basis of the range and consistency rules built into the data entry dictionary. The validation procedure created a query file, from which query sheets were printed. Each query was first checked against the data form, and if it was not a data entry error, i.e., the flagged data were as recorded on the data form, it was sent to the interviewer for investigation. It was necessary in some instances to revisit the respondents to obtain correct information. When data were confirmed to be correct despite the queries, the interviewer indicated this and no correction was made. When corrections were necessary, they were recorded on the data form and the query sheet. The query sheets with corrections were handed back to the data management unit, where the data manager created a correction batch to update the master file.

All master file updates and corrections were carried

out using transaction batch files and correction files, respectively. The procedure for updating master files included a compulsory step in which backup copies of the old master files and the transaction files were saved. The output report was checked after each update to assess whether the procedure had been successfully completed, and if there were any problems, such as duplicate records in the new master file, or if some records in the batch had been rejected in the updating process. The latter occurred if a record with duplicate identification had already been saved in the master file. To correct data errors and delete duplicate or faulty records, correction statements were processed against the master file with the same backup requirements and output listings, as described for adding new records to the master file. Interactive correction of the master files was not permitted, which, together with the careful documentation of queries and corrections, helped to maintain a clear data audit trail. Moreover, in the event of a computer crash, the master files could be recreated by rerunning the transactions and updates in their right order.

The batches were dismantled once the data forms had been processed through to master file updating. At this point, the processing history from the batch cover form was copied into the batch log register, the batch cover form was filed away, and the data forms were stored in the individual subject folders kept in the archiving unit for each study participant.

### **Standard operating procedures at the Coordinating Centre**

The Coordinating Centre had the same software and the same electronic questionnaire dictionaries as the sites, making it possible to replicate some of the site procedures. For the first six months of data management, sites sent their monthly returns in the form of transaction files. The Coordinating Centre replicated the validation and update of these files to evaluate each site's compliance with the SOPs. After the initial period of six months, only master files were transferred to the Coordinating Centre. A log was kept of all data received, and master file update listings were used to double-check that the Coordinating Centre had exact copies of the master files kept in each respective site.

The different master files were combined at the Coordinating Centre to create an analysis file (separate for longitudinal and cross-sectional studies) in which each subject had a single record with aggregate data from separate questionnaires. Data from repeating forms (e.g., the 20 follow-up forms) were reorganized to create only one record per subject instead of having a record for each follow-up visit. The data were thus arranged in suitable format and structure for analyses using standard statistical software programs. This

process also permitted further validation checks for consistency among data originating from different master files, e.g., measurements changing abnormally relative to the chronology of follow-up visits, or visit dates that were inconsistent with the sequence of visits. Derived variables were created from existing variables; for example, in the longitudinal study a feeding compliance indicator was derived from data on breastfeeding and complementary food intake recorded at different follow-up visits.

Descriptive statistics and data plots were also routinely studied to identify data problems. Queries about inconsistent and dubious data were fed back to the site to investigate and implement any required corrections. As with locally generated queries, the interviewers returned to the forms and sometimes to the respondents to verify queried data. Documentation of these queries and the responses to them were kept on file at both the site and the Coordinating Centre. When queries could not be adequately resolved through e-mail correspondence, they were reviewed on site during monitoring visits that were undertaken annually by a member of the Coordinating Centre team.

In addition to quality control checking and interacting with sites to resolve data problems, the Coordinating Centre also produced reports that were used to monitor sample recruitment and retention, and, in the longitudinal study, compliance with MGRS feeding recommendations and smoking restrictions. Detailed monitoring reports were produced periodically to inform the Executive Committee and the Steering Committee of the progress of the study.

During the data collection phase, summary statistics were produced to evaluate each interviewer's digit preference in anthropometric measurements. Significant digit preferences were studied to determine if they might lead to overall biased measurements and were communicated to the site for discussion with the relevant interviewers. The frequency of measurements that had been repeated because the maximum allowable differences between observer pairs had been exceeded was also monitored to assess adherence to the Measurement and Standardization Protocols of the MGRS [7].

### Closure of data management activities

After data collection was completed in a given site, a period of about six months was dedicated to in-depth data quality checking and master file cleaning. The Coordinating Centre produced detailed validation reports, descriptive statistics, and plots from the site's master files. For the longitudinal study, each anthropometric measurement was plotted for each individual child from birth to the end of his or her participation. These plots were examined individually for any questionable patterns. Query lists from these

analyses were sent to the site for investigation and correction or confirmation as required. As with the data collection process, the site data manager prepared correction batches to update the master files. The updated master files were then sent to the Coordinating Centre, and this iterative quality assurance process continued until the site and the Coordinating Centre were satisfied that all identifiable problems had been detected and corrected.

At this point, a team from the Coordinating Centre carried out a data management closure visit with the following objectives: to clean up any outstanding data problems and document those that could not be resolved; to certify the site's adherence to the data management SOPs; and to produce the final site data set, list closure analyses, and archive all study materials.

Any pending data errors were corrected during the visit, and those that could not be resolved were documented, such as observations flagged as out of the probable range but confirmed to be correct. Clerical procedures for handling data collection forms as well as computer procedures for handling the data in the electronic files were reviewed and documented. Finally, a set of descriptive analyses was run on the final data set, and the results were reviewed with the site team. An inventory of all study materials was made, and the location of their storage and their retention period were discussed with the site team and documented. The final site master files were archived, and copies of the same were sent to the Coordinating Centre for inclusion in the MGRS master data set.

Closure of data management activities meant that master files were henceforward frozen and therefore not to be changed by either the site or the Coordinating Centre. Any problems identified thereafter could only be dealt with and documented at the analysis stage. The final master file copies and other study documentation were kept in read-only format at the Coordinating Centre with CD-ROM backups of the same.

### Discussion

Among the criteria applied in selecting sites for the MGRS were the existence of local expertise and the capacity to implement the study. The need to have personnel with adequate skills and computing facilities for data management was integral to this criterion. In addition, the data manager from each site received specific training in implementing the MGRS data management protocol and using the centrally prepared computing system. Each site had at least two computers dedicated exclusively to data management. The staff involved had variable data management experience, but since all sites used a standard package, those that experienced problems received technical support from the Coordinating Centre or the data managers from other sites whenever

required. For example, the first data manager in Ghana left before the study began, and her replacement was trained on-site by the Norwegian data manager.

The setup and operation of the system were designed to ensure the accumulation of high-quality data and to secure them against unauthorized manipulation and accidental loss. We chose to decentralize data handling rather than use a centralized model in which all data would have been sent to the Coordinating Centre for entry, verification, validation, and creation of the primary master files [8]. The chosen organizational model had the advantage of fostering capacity building in the sites and provided a framework for intersite technical support. The decentralized system also kept the questionnaire forms close to the data sources, which minimized the risk that data would be damaged or lost and made the process of verifying queried data efficient, especially when it was necessary to revisit the respondents. Few problems were experienced over the years in transferring data through the Internet, and these were minor, easily resolved ones, such as corrupted files. The sites kept their reporting schedules throughout data collection, which facilitated the Coordinating Centre's task of ensuring that the central master files were up-to-date with the site master files. It also helped the timely detection of problems that could only be revealed when data from separate master files were combined in the analysis file, so sites could be alerted to investigate them within weeks of the initial data entry.

Data management in the longitudinal study in Brazil proceeded differently from the process described in this article, because the site began data collection well ahead of the others (in July 1997) and served to pilot test the MGRS protocol and questionnaires [1, 2]. This head start also explains why Brazil did not have forms for breastfeeding and motor development data (table 1), as decisions to collect and record these data were taken after this site had initiated data collection [1]. The first data management workshop was conducted in Geneva

in November 1998, by which time Brazil was in the second year of the longitudinal follow-up. The data from that site had therefore to be converted from Epi Info [9] to the DMS/2 system for incorporation into the MGRS master files. The conversion process was achieved with the Coordinating Centre's assistance over the Internet and a site visit to Brazil by the Norwegian data manager. Once the data files were converted to DMS/2, they were subjected to the same in-depth validation and quality checking that was standard for the other MGRS sites. The cross-sectional study data were collected using the centrally prepared questionnaires and computer processed using the standard package.

The inbuilt range and consistency checks of the computerized system, as well as the ongoing data monitoring routines at the Coordinating Centre, were highly effective in detecting data errors, and since data cleaning kept pace with data collection and entry, most problems were detected and corrected soon after the data had been computerized at the site or received at the Coordinating Centre. The emphasis on keeping a clear audit trail in all data handling also helped in identifying sources of problems and taking appropriate measures to strengthen the quality assurance system.

The multiple tiers of data checking steps may have been too labor-intensive for some sites, but where routine might lead to errors being overlooked, the possibility of their detection was provided by the next checking level. Individual anthropometry plots were checked at the end of data collection in each site, and hence a few data errors were detected long after the data were collected. These very few obviously erroneous measurements that could not be corrected were excluded from the analysis file. Overall, however, the site and Coordinating Centre data management teams implemented the data management protocol with a high degree of rigor, and the MGRS data set is of very high quality.

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# Implementation of the WHO Multicentre Growth Reference Study in Brazil

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) South American site was Pelotas, Brazil. The sample for the longitudinal component was drawn from three hospitals that account for approximately 90% of the city's deliveries. The cross-sectional sample was drawn from a community survey based on households that participated in the longitudinal sample. One of the criteria for site selection was the availability of a large, community based sample of children whose growth was unconstrained by socioeconomic conditions. Local work done in 1993 demonstrated that children of families with incomes at least six times the minimum wage had a stunting rate of 2.5%. Special public relations and implementation activities were designed to promote the acceptance of the study by the community and its successful completion. Among the major challenges of the site were serving as the MGRS pilot site, low baseline breastfeeding initiation and maintenance rates, and reluctance among pediatricians to acknowledge the relevance of current infant feeding recommendations to higher socioeconomic groups.*

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

Mention of the names of firms and commercial products does not imply endorsement by the United Nations University.

**Key words:** Anthropometry, Brazil, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, infant feeding practices

## Introduction

The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) South American site was Pelotas, Brazil. Pelotas is in the state of Rio Grande do Sul in the southernmost region of Brazil. The city has approximately 330,000 inhabitants. It has a highly experienced Epidemiology Research Center, with internationally recognized expertise in longitudinal studies of maternal and child health nutrition [1, 2].

Among the site selection requirements for the MGRS was that social and environmental conditions experienced by the study sample permit unconstrained growth in early childhood [3, 4]. Data from all children born in Pelotas in 1993 [2] were analyzed to identify a socioeconomic cutoff above which children in Pelotas have a prevalence of stunting of 2.3% based on the current international reference [5]. These analyses demonstrated that children in this community from families whose monthly incomes are at least six times the minimum monthly wage (approximately US\$600) have a stunting rate of 2.5% [6]. This cutoff was used to define socioeconomic eligibility for the sample from this site.

Breastfeeding rates were known to be low from previous research conducted by the research team. However, their experience also demonstrated that baseline breastfeeding initiation and continuation rates could be improved substantially with adequate breastfeeding promotion.

This site piloted the MGRS protocol, and its experiences were of particular value in the implementation of the study in other sites.

## Planning phase

### Study timeline and preparatory activities

The MGRS protocol is summarized elsewhere in this supplement [3]. The study timeline of the site is summarized in figure 1.

The required sample size necessitated the successful recruitment of approximately 6 infants per week to achieve a longitudinal sample size of 300 within 12 consecutive months. The 1993 study [6] referred to above was used to estimate the prevalence of other MGRS exclusion criteria within the group of mothers whose income met or exceeded the socioeconomic criterion used to define eligibility (table 1).

The sample for the longitudinal component of the study was recruited from the Santa Casa de Misericórdia, Beneficência Portuguesa, and São Francisco de Paula hospitals. The three hospitals were visited by the study coordinator to explain the objectives of the study and procedures and request authorization for data collection in each facility. A meeting was held for all pediatricians practicing in the city to explain the goals of the study and request their collaboration, especially concerning the promotion of breastfeeding. Letters also were sent to each participating child's pediatrician asking for their support and offering lactation counseling services to their practices.

TABLE 1. Prevalence estimates of exclusion criteria based on the cohort of children born in Pelotas, Brazil in 1993

Exclusion criterion	Prevalence (%)
Gestational age less than 37 weeks	7.3
Maternal smoking	23.8
Admission to intensive care unit	2.2
Admission to nursery ward	3.2
Twin birth	2.3
Nonintention to breastfeed for at least 12 months	25.9
Any of the above	50.2

Institutional ethical approvals were obtained from the Ethical Committee of the Federal University of Pelotas.

### Study teams

Six teams were set up to implement the longitudinal and cross-sectional components of the study: the screening, lactation counseling, follow-up, cross-sectional, coordination, and data management teams. The composition and coordination of the teams are summarized in figure 2. Participation in any team was not exclusive, so, for example, the same interviewers

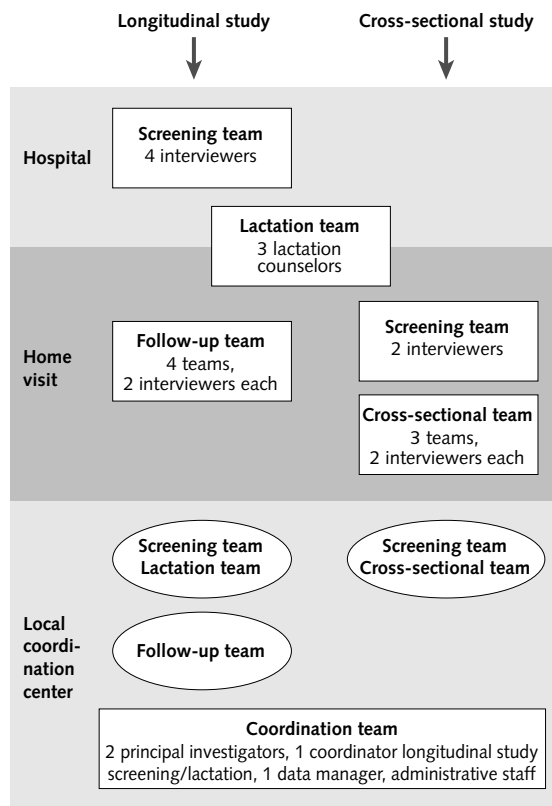


FIG. 2. Composition and coordination of study team

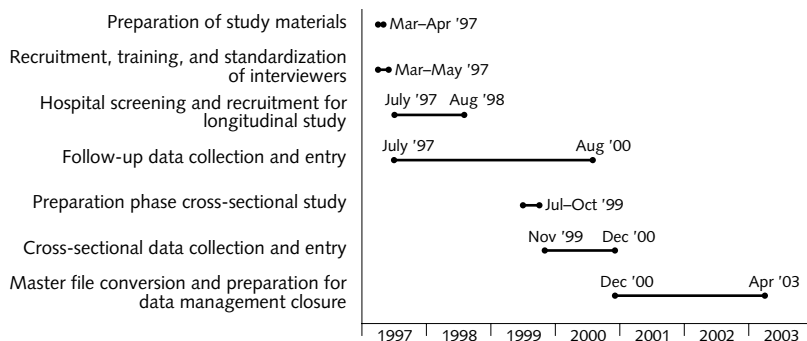


FIG. 1. Study timeline

participated in the longitudinal and cross-sectional components of the study. All follow-up and cross-sectional team interviewers worked full-time on the project. With one exception, all had college degrees, six of them in nutrition.

The screening team, composed of four interviewers and one supervisor responsible for quality control in the hospitals and for reviewing the questionnaires for completeness and accuracy, was in charge of screening all mothers in the hospitals to determine eligibility. The lactation counseling team included a senior lactation consultant and three registered nurses, one of whom made the first visit while the mother was in the hospital. The follow-up team included four groups of two interviewers each and one fieldwork supervisor. The cross-sectional team included two screeners and three pairs of interviewers. At the coordination level there were two local principal investigators (one of whom coordinated the follow-up and cross-sectional studies), one coordinator for the screening and lactation teams, and two administrative staff members. The data management team was composed of one data manager and two data entry clerks.

### **Training and initial standardization**

Fourteen female candidates were screened. After detailed explanations of the project and anthropometric training had been provided to each of them, 11 were recruited. Each of the 11 team members participated in the initial anthropometric standardization session conducted by one of the two WHO-designated lead anthropometrists. Based on the results of this standardization session, the eight interviewers who performed best were selected.

Members of the lactation support team completed the 40-hour WHO lactation support training course [7]. This course was provided by two International Board Certified Lactation Consultants.

### **Adaptation of study materials and procedures**

Brazil was the first country to begin data collection; the original forms and operational manuals for the longitudinal study were developed in Portuguese for pretesting at this site. They were later translated and adapted by the other MGRS sites, as described in the methodological paper in this supplement [3]. The instruments for the cross-sectional component were written originally in English, and therefore the standard translation procedure was used in adapting them [3].

The reluctance of some mothers to undress their infants completely for weighing in winter was anticipated. Therefore, samples of children's clothes were weighed and a list of clothing weights was prepared. This list was used to correct weights of partially or

completely dressed children. A similar list was compiled for parents' clothing. A list of the main brands of infant formulas used by this community was also prepared for coding nonhuman milk intakes. A list of vitamin and mineral supplements was developed to help mothers identify the brand names of products they used and/or provided to their infants.

### **Public relations activities**

The success of the study required the close collaboration of the city's hospitals, doctors, and families. This required that attention be paid to public relations activities. These activities included visits to the three hospitals involved by the study coordinators, with lectures on the rationale for the study and the need to promote and support breastfeeding; donation of medical textbooks to the hospitals; breastfeeding lectures, to which all pediatricians in the city were invited; an initial study newsletter that included reprints of WHO Feeding Recommendations [8]; distribution of breastfeeding promotion leaflets to all mothers giving birth in the study hospitals (whether or not they fulfilled the eligibility criteria); regular newsletters to all pediatricians and other doctors of participating families that included breastfeeding information and feedback from the study; study advertisements in local newspapers; and regular publication of articles on the study and/or breastfeeding in local newspapers.

Maintaining excellent rapport between interviewers and families was viewed as essential to the success of the study. The role of the interviewer's attitude and perceived friendliness and helpfulness was stressed. Small gifts, such as infant participation diplomas on which infant weights were recorded and a photo album delivered at the infant's first birthday, were also designed to demonstrate to families how much their help was appreciated. Additionally, on their second birthday, children who participated in the longitudinal study received a T-shirt with the WHO logo and the statement "I participated in the International Multicentre Growth Reference Study."

## **Implementation of the longitudinal study**

### **Sampling strategy**

All women who resided in Pelotas and delivered at one of the three hospitals listed above, who gave birth to a full-term singleton, and whose baby was not admitted to a nursery or child intensive care unit for more than 24 hours were interviewed from July 1997 to August 1998. For convenience, only deliveries taking place between 6 pm Sunday and 6 pm Friday were screened. Analyses of the 1993 cohort data set showed no differ-

ences between babies born on weekdays and weekends (e.g., in rates of vaginal deliveries).

### Screening and enrollment of children

All enrolled infants met the eligibility criteria outlined in the MGRS protocol [3]. Other selection criteria specific to this site are shown in table 2. The exclusion criterion “mother planning to stop exclusive breastfeeding before four months” in the MGRS protocol was not applied, because local data showed that the intended duration of exclusive breastfeeding—as reported soon after delivery—is unrelated to actual duration. Estimates of gestational age were based on ultrasound measurements; the interviewers carried gestational age calculators to assist with this estimate. The study supervisor subsequently checked all calculations [9]. If no ultrasound examination was available, the date of the last menstrual period was used to estimate gestational age. If neither the last menstrual period nor an ultrasound examination was available, and the child fulfilled all other eligibility criteria, the screening coordinator (a pediatrician) was contacted immediately. The pediatrician estimated the infant’s gestational age by the Dubowitz method [10].

At the end of the interview, mothers with eligible infants were invited to participate in the study. Consent obtained in the hospital was regarded as preliminary. Written consent was obtained during the first home visit.

### Follow-up logistics

Pelotas was subdivided into four areas. Each was assigned to a pair of interviewers on the follow-up team. The four pairs of interviewers conducted follow-up visits and obtained all measurements for the longitudinal component of the study. Each team was organized so that one of the interviewers was fixed and the other was rotated every two months. This rotation among teams was designed to minimize systematic errors caused by reinforcement of faulty techniques and also allowed the comparison of measurements among distinct interviewer pairs. The consistency of

one interviewer visiting any given subject helped ensure good rapport with mothers and children.

During the first home visit, at 14 days, the interviewers explained the schedule and methods of the study to the mothers and the importance of their participation. The study forms completed in the follow-up visits have been described elsewhere in this supplement [3]. The interviewers returned the completed questionnaires to the local coordination center twice a week.

Decisions by one or both parents to leave the study were reported immediately to the study coordinator, who immediately contacted the mother to review the reasons for this decision. The coordinator outlined the requirements of the study to ensure that the decision was a well-informed one.

To assess the possibility of selection bias, it was important to have information on mothers and infants who refused to participate or who dropped out of the study [3]. Attempts were made to locate by telephone the families of all children who were designated as eligible during the hospital screening, but who, for various reasons, were not participating at age 12 months. A home visit was scheduled for all who consented to participate in the 12-month study [3].

### Lactation support team and complementary feeding

In addition to the initial hospital lactation counseling visit, the lactation support team made home visits at 5, 15, 30, and 45 days and at 2, 3, 4, 6, 8, 10, and 12 months after delivery. Extra visits were conducted whenever there were problems requiring further attention, such as cracked nipples. Telephone calls were made at 5, 7, 9, and 11 months after delivery to assess how breastfeeding was proceeding. Additional visits were scheduled on the basis of these inquiries.

The first hospital visit included advice on the advantages of breastfeeding; nursing was observed, and correction of the baby’s position was advised if necessary; instructions on how to express milk manually were given, and a breastfeeding promotion leaflet was distributed. The home visits included the same content. When the infant was six months of age, the mother received advice on the need to introduce complementary feeding, and on recommended foods [8] (table 3).

One lactation counselor was assigned to each mother throughout the study. On average, each lactation counselor was responsible for visiting two newly enrolled mothers per week. The lactation support team coordinator visited each enrolled mother at least once during the study. She also accompanied lactation counselors in their visits whenever there were particularly difficult lactation problems.

A telephone hotline was maintained 24 hours a day, seven days a week, to assist mothers who experienced

TABLE 2. Longitudinal study selection criteria specific to the Brazilian site

Criterion	Operationalization
Perinatal morbidity	Absence of significant perinatal morbidity (newborns with postnatal stay in intensive care > 24 hours excluded)
Intention to breastfeed	Mothers who expressed intention to breastfeed, regardless of duration
Socioeconomic criteria	Family income at least US\$600 per month



TABLE 3. Complementary feeding guidelines at the Brazilian site

Age (mo)	Recommendations
0–5	Breastfeed Do not give teas, water, or other types of milk or food
6–11	Breastfeed Introduce complementary foods, with emphasis on Meat Eggs Fruits and vegetables (mainly yellow) Mashed beans Avoid diluted foods with high water content Use cup and spoon, not baby bottles Start with 1 complementary feed per day and increase to 3 feeds per day
12–23	Breastfeed Give complementary foods at least 5 times a day Family foods should be the main type of food

particularly severe problems. The hotline number was provided to all mothers and to their pediatricians.

## Implementation of the cross-sectional study

### Sampling strategy

The cross-sectional study was designed as a “panel study” in which children aged 18 to 71 months were enrolled and visited up to three times, at three-month intervals. This was aimed at increasing the number of available measurements. Children who reached the age of 72 months during the implementation of the cross-sectional study were visited only once or twice.

The sampling strategy of the cross-sectional component was designed to obtain a sample of children aged two to five years who were similar to children enrolled in the longitudinal component. To accomplish this aim, the addresses of children taking part in the longitudinal study were plotted on a city map. The homes of index children were used as points of departure for identifying participants in the cross-sectional component. The interviewers were instructed to move in a clockwise direction relative to the index child’s household. The interviewers visited all houses or apartments on blocks shared by the index households until three children within the required age group were located. If three eligible children were not located in the first block, the interviewers moved to another previously defined block in the same neighborhood. The neighbors were asked to provide information concerning any child

under age 10 living in homes with whom contact could not be made. The age of 10 was selected to provide a margin of safety in order not to miss potentially eligible children. If two different neighbors provided consistent information that no children under 10 lived in the targeted home, the home was excluded. In doubtful cases, the interviewers revisited the home in question. When children aged 18 to 71 months were identified, a screening questionnaire was administered to a responsible caregiver. If the child fulfilled all eligibility criteria, the mother or guardian was invited to participate in the study. Appointments for consenting children were made to obtain anthropometric measurements. Children who were enrolled or had participated in the longitudinal component of the study were ineligible for the cross-sectional component.

## Standardization, quality control, and data management activities

### Standardization sessions

Anthropometry standardization procedures followed the MGRS protocol [11]. Initial practice sessions were conducted at two municipal day-care centers. Subsequent anthropometric standardization sessions were conducted with 17 children under three years of age at one of the two day-care centers in which initial training was conducted. Each of the study anthropometrists measured the same child twice, as did the local lead anthropometrist. The local lead anthropometrist’s measurements were regarded as “reference values.” Nineteen standardization sessions were carried out, one every two months, in addition to the initial standardization session held by one of the two WHO-designated MGRS lead anthropometrists. Intra- and interobserver technical errors of measurement (TEM) were calculated for each fieldworker from data collected in these standardization sessions.

The motor development component of the MGRS was not performed at this site, so no standardization sessions related to this component were scheduled.

### Quality control activities

The interviewers returned the completed questionnaires to the site’s coordinating center within four days of all interviews. The questionnaires were reviewed and open questions were coded by the relevant team’s supervisor. Problems encountered at this stage were discussed at the next team meeting to permit the group to review all discrepancies, allow agreement to be reached on how each discrepancy should be resolved, and identify how best to prevent the recurrence of similar problems. After appropriate follow-up was

completed, any required corrections were made, and the questionnaires were forwarded to the data manager for double data entry. Team meetings were scheduled at two-week intervals throughout the study.

Quality control questionnaires that repeated questions about morbidity, vitamin or mineral supplement intake, maternal work, and child feeding were administered to 20% of mothers visited each week. To determine which mothers would be reinterviewed, a list with the numbers of the questionnaires completed during the week was prepared, and 20% were selected randomly. The quality control interview was carried out by telephone by the quality control staff, one to two days after the actual interview.

Calibration of equipment was conducted as outlined in the MGRS measurement and standardization protocols [11].

### Data management

Data management in Pelotas differed from that at other MGRS sites. This was partly because Pelotas served as the MGRS pilot site. Data collection was started before data entry routines used in the other sites had been fully developed at the WHO Coordinating Centre in Geneva.

All databases in the longitudinal study were originally created using Epi Info software [12]. All data were entered twice; comparison of the two files allowed the correction of data entry errors. Data cleaning procedures were conducted separately for each file. In order to adapt these databases to the MGRS master file structure, all variables were renamed and reformatted using SPSS 8.0 for Windows software. After this process, all data files were satisfactorily incorporated into the master files at the WHO Coordinating Centre [13].

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### Conclusions

The MGRS is a complex study that required careful planning and implementation. The research team in Brazil gained much experience both from the methodological aspects of this study and from interaction with the other participating centers. The site's major challenges were related to breastfeeding. The lactation support team experienced the greatest turnover, and securing the adherence of local pediatricians to the feeding recommendations of the study was often difficult. The high turnover of the lactation support team was probably a result of team members' clinical responsibilities related to their ancillary nursing duties. These affected their availability to make home visits to, and receive telephone calls from, participants who experienced breastfeeding problems.

Another important challenge was that some of the city's pediatricians were not supportive of current feeding recommendations. Mothers were often encouraged to administer teas, water, and/or juice to their infants starting at one week of age. The pediatricians often recommended formula feeding at the earliest sign of any breastfeeding difficulty. Pediatricians also commonly had little, if any, knowledge about lactation support. Letters, reprints and other educational material sent to selected physicians were inconsistently effective in changing practices. It was not uncommon for mothers to contact a lactation consultant immediately after appointments with their pediatricians to check if advice they had just received was consistent with the recommended practices of the study. Despite these constraints, lactation support was highly successful: whereas prior to the study about 18% of mothers who fulfilled the inclusion criteria breastfed for one year, this proportion almost doubled in the MGRS.

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# Implementation of the WHO Multicentre Growth Reference Study in Ghana

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) African site was Accra, Ghana. Its sample was drawn from 10 affluent residential areas where earlier research had demonstrated the presence of a child subpopulation with unconstrained growth. This subpopulation could be identified on the basis of the father's education and household income. The subjects for the longitudinal study were enrolled from 25 hospitals and delivery facilities that accounted for 80% of the study area's births. The cross-sectional sample was recruited at 117 day-care centers used by more than 80% of the targeted subpopulation. Public relations efforts were mounted to promote the study in the community. The large number of facilities involved in the longitudinal and cross-sectional components, the relatively large geographic area covered by the study, and the difficulties of working in a densely populated urban area presented special challenges. Conversely, the high rates of breastfeeding and general support for this practice greatly facilitated the implementation of the MGRS protocol.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, Ghana, growth, growth monitoring, growth references, infant feeding practices

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

## Introduction

The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) African site was Accra, Ghana. Ghana is in the West Africa subregion, has a population of 18.3 million [1], and lies 420 km north of the equator. It has two main seasons: the wet season, which peaks from April to June, and the dry season between November and March.

Inclusion of the Ghanaian site was dependent on identifying a subpopulation of children with no socioeconomic constraints on growth. Government property valuations were used to identify 10 communities in the most affluent areas of Accra: the Airport Residential area, Atomic, Adenta, Cantoments, Dansoman, Dzorwulu, East Legon/Legon, Manette/Sakumono/Lashibi, Roman Ridge, and Tema. They were surveyed to assess the feasibility of conducting the MGRS [2]. Households with children aged between 12 and 23 months were identified; information on household demographic and socioeconomic characteristics was collected; and anthropometric measurements of the children, their mothers and grandmothers were obtained. This information was used to identify socioeconomic factors associated with unconstrained growth in early childhood. Information was also collected on hospitals and other delivery facilities used by women in the selected residential areas.

The survey identified the socioeconomic characteristics associated with unconstrained growth of children from affluent families to be high level of education (tertiary) of the father and household income [2]. Having met the criteria required of participating sites [3], Accra was selected as the African MGRS site. Twenty-five hospitals and other delivery facilities were identified that accounted for 80% of births in the targeted subpopulation. The subjects were recruited from those sites. The objective of this paper is to provide an overview of the implementation of the MGRS at the Ghanaian site.

## Planning phase

### Study timeline and preparatory activities

The MGRS protocol is described in detail elsewhere in this supplement [3]. The timeline for its implementation in Accra is summarized in figure 1. The preparatory phase lasted from June to October 1999; data collection for the longitudinal component of the study was initiated in December 1999 and completed in December 2002. The cross-sectional component lasted from November 2001 to May 2003.

The principal investigators and/or one of the other members of the research team visited each of the 25 hospitals and other delivery sites to discuss the aims and procedures of the study. Letters were also sent to each hospital formally seeking permission to recruit infants. All gave written consent, except for one facility whose director gave oral consent. Each facility identified one or two maternity ward nurses to serve as contacts between the project and the delivery ward. These senior maternity ward nurses in charge of deliveries enabled the project to identify all deliveries within the required 24 hours after birth.

Institutional approvals were obtained from the University of Ghana Medical School Ethical Review Committee.

### Study teams

The site had four study teams: coordination, screening, lactation support, and follow-up. The positions for all field research assistants were advertised in the University of Ghana. Qualified applicants were interviewed and recruited based on their motivation, communication skills, dedication to work, and ability to work in a team.

The coordination team consisted of the two principal investigators, lactation supervisors, a quality control

manager, a data manager, a project secretary, and a project adviser. The coordination team was responsible for the overall administration of the study.

The screening team was made up of six members, all with undergraduate university degrees in nutrition or nursing. This team was hospital based and was responsible for the identification and screening of newborns for eligibility and for obtaining initial anthropometric measurements of enrolled subjects. The screening team worked five days a week (Monday to Friday).

The lactation team was made up of 10 senior or principal nursing officers working with the Ghana Health Service. Each had successfully completed the WHO lactation management and breastfeeding counseling course [4] before the MGRS was implemented in Ghana. Each also used the knowledge and skills gained through that training in their usual employment. The lactation counselors assisted newly delivered mothers to initiate breastfeeding successfully in the hospital, encouraged mothers to comply with the feeding recommendations of the study, and helped them solve any breastfeeding problems that they experienced. They administered the breastfeeding questionnaires and obtained infant weights at the first home visit. The lactation counselors worked part-time; however, the mothers could call their assigned lactation counselors or the lactation team supervisor 24 hours a day, seven days a week.

The follow-up team was made up of six individuals, all with undergraduate degrees in nutrition. The team was responsible for home visits. They administered baseline and follow-up questionnaires and took anthropometric measurements of children and parents. The team normally worked from Monday to Saturday. Some home visits were scheduled on Sundays to ensure the father's availability. The same follow-up interviewers participated in the longitudinal and cross-sectional components of the study. Figure 2 shows the coordination of study teams.

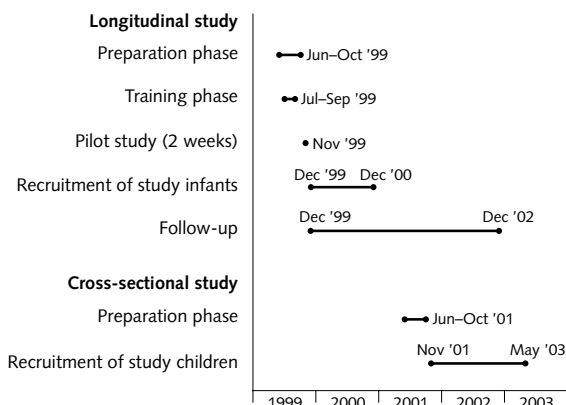


FIG. 1. Study timeline

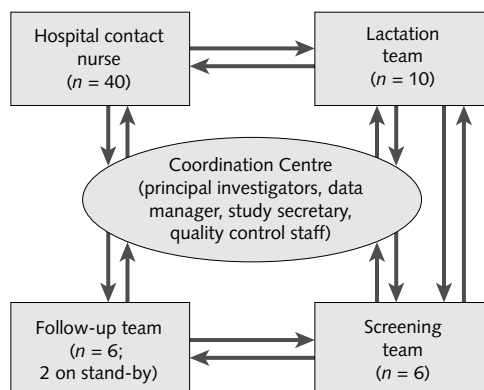


FIG. 2. Study team coordination chart

### Training and initial standardization

A one-day workshop was held for all nurses serving as project contacts to review the project's goals and procedures and their respective roles in its successful implementation. The field research assistants' training included a review of the background and objectives of the MGRS, the administration of questionnaires, and the standardized use of study forms and interviewer guides. Particular attention was given to the estimation of gestational age, which was calculated on the basis of ultrasound or estimated from the last menstrual period. The interviewers were trained in the use of "gestograms" [5] using the last menstrual period as the base for the calculation. Follow-up interviewers also conducted role playing sessions at participating maternal and child health clinics to hone interviewing skills. A counseling expert provided training in interviewing techniques and reviewed culturally acceptable behaviors to be observed during home visits.

Anthropometric training and standardization followed the MGRS procedures [6]. Practice sessions on the proper handling of newborns were conducted at one of the participating hospitals, and the screening team received practical training in obtaining measurements on newborns. The follow-up team practiced anthropometric measurement techniques on children attending growth monitoring and immunization clinics. Before the start of data collection, the anthropometry teams participated in a formal standardization session involving one of the two WHO-designated lead anthropometrists, as described elsewhere in this supplement [6]. Team members whose measurements were characterized by low accuracy and/or precision were given corrective training. After this initial standardization with the WHO-designated lead anthropometrist, six screening and six follow-up interviewers were selected for the initial teams. Two adequately trained interviewers were selected as backups. The anthropometry standardization sessions were repeated every two months, separately for the screening and follow-up teams, with the participation once a year of the WHO-designated lead anthropometrist.

Selected interviewers were also trained by staff from the MGRS Coordinating Centre in Geneva to assess the achievement of the six motor developmental milestones, following the MGRS protocol [7].

The training of the lactation support team members for the study focused on providing support to mothers in fulfilling the MGRS feeding requirements [3], administering the breastfeeding questionnaires, and measuring mothers' and babies' weights at the week 1 visit.

Three weeks before data collection was initiated, a two-week pilot study was conducted to test the logistics of the site. The 25 hospitals and other delivery facilities from which subjects would be recruited were grouped

into three clusters of nine, nine, and seven. One pair of screeners was assigned to each cluster. The pilot study demonstrated that Accra's heavy traffic would be a major challenge. On the basis of these experiences, the screening teams were required to start their day no later than 7 am, and the clustering of hospitals and other delivery facilities was reorganized to avoid heavy traffic areas.

### Adaptation of study materials and procedures

The generic Manual of Operations was adapted to the circumstances of the site with the assistance of the WHO Coordinating Centre, as described elsewhere in this supplement [3]. The eligibility criteria specific to the Ghana site are shown in table 1. This site did not use nonintention to breastfeed as an exclusion criterion, since breastfeeding is nearly universal in Ghana. At our site it was not necessary to translate the study questionnaires into local languages. The mothers enrolled in the study all spoke English fluently, as would be expected in this socioeconomic group. Therefore, all interviews were conducted in English.

### Public relations activities

Several public relations activities were undertaken to enhance community acceptance and help ensure the successful implementation of the study. The project was launched officially by the Deputy Minister of Health, the Vice-Chancellor of the University of Ghana, and representatives of WHO and UNICEF in Ghana. Health-related organizations, physicians, and nurses from all participating hospitals and the media were present. The Deputy Minister of Health awarded a baby diploma to the first mother recruited to the study. The local principal investigators also appeared on popular television and radio programs to present the MGRS project to the public.

Breastfeeding information and other leaflets describing fathers' roles in supporting their breastfeeding wives were provided to subjects and their families. Each infant was presented with a baby participation diploma and a bib with the project's logo. At one year of age, all study infants were given personalized birthday cards and an educational toy. At two years, each child

TABLE 1. Eligibility criteria for enrollment of children at the Ghanaian site

<p><i>Absence of significant perinatal morbidity (newborns with postnatal stay in intensive care &gt; 24 hours excluded)</i></p> <p><i>Socioeconomic criteria:</i></p> <p>Father has polytechnic education and income &gt; 1 million cedis</p> <p>Father has university education and income &gt; 200,000 cedis</p>
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1 US\$ = 2,300 cedis (exchange rate July 1998).

received a book.

For the cross-sectional study, day-care center heads or directors were invited to attend a one-day workshop. Its purpose was to explain the goals and objectives of the MGRS cross-sectional component and the roles they and their centers could play. The keynote speaker at the workshop was the Deputy Minister of Education. He encouraged all the centers to support the project.

## Implementation of the longitudinal study

### Sampling strategy

The average number of monthly deliveries in the 25 participating hospitals and other delivery sites was about 1,276. A successful recruitment rate from that pool of less than 10% was anticipated, based on the expected prevalence of exclusion criteria and refusals among women delivering at the various sites. A recruitment rate of 6 or 7 children per week was necessary to meet the project's target of recruiting 300 eligible infants in one year. Thus, all infants born in the 25 study hospitals and other delivery facilities whose parents resided in the study areas were screened.

### Screening and enrollment of children

Hospital contact nurses assisted in identifying potentially eligible mothers. Using a simple one-page pre-screening form, the contact nurse asked prospective subjects if they lived in any of the study areas and inquired about the husband's years of formal education. If both criteria were met, the mothers and their infants were considered potentially eligible. In cases where the mothers were uncertain about their husband's educational level, residence in one of the designated areas was sufficient to establish potential eligibility. Contact nurses were asked to report potentially eligible mothers to the site's coordination office. Unfortunately, not all contact nurses were equally cooperative. To compensate for this, the screening teams visited all 25 hospitals and other delivery facilities at intervals of less than 24 hours. The hospital with the highest number of daily births was visited twice daily, in the morning and late afternoon.

Subjects for whom no preliminary exclusion criterion was identified were interviewed by the screening team, and newborn anthropometric measurements were obtained. Eligible mothers who were willing to participate in the study gave oral consent at the hospital.

### Follow-up logistics

Each enrolled subject was assigned a pair of follow-up interviewers. Each subject was visited consistently by

one member of each pair; the other member of the pair was rotated among other follow-up teams every two months, after each bimonthly (every two months) anthropometric standardization session [3].

At the first follow-up home visit, the study was reviewed with mothers and their husbands, if present, and written consent to participate was obtained at this time. This visit also provided a second opportunity to confirm the mother's and infant's eligibility. Mothers who were enrolled at the hospital visit but were found not to have complied with study feeding recommendations or not to have conformed with other inclusion requirements were classified as "hidden ineligibles." Those who remained eligible but rescinded their decision to participate were classified as "hidden refusals." Hidden ineligibles and hidden refusals were excluded from the study and replaced in the sample following the MGRS protocol [3]. Eligible mothers who dropped out of the study after the first follow-up visit were requested to consent to one measurement when the child reached 12 months.

The motor development study and the 12-month follow-up visit of refusals and dropouts were conducted in accordance with the MGRS protocol [3, 7].

### Lactation support and complementary feeding

The enrolled mothers usually received the first lactation support visit in the hospital. In cases where this was not possible, they were visited no more than three days after discharge. After this initial visit, the lactation support team made home visits at one and two weeks and at three and six months, as specified in the MGRS protocol. However, extra visits were scheduled at one and two months for primiparous mothers and for mothers who had breastfeeding problems at weeks one and two. Between three and six months, no extra visits were scheduled except when requested by the mother.

The mothers were advised to introduce complementary foods to the infant by six months of age. The complementary feeding guidelines, shown in table 2, were developed by the Nutrition Unit of the Ghana Health Service [8]. These guidelines were developed to facilitate the activities of field extension workers involved in nutrition education.

## Implementation of the cross-sectional study

### Sampling strategy

A summary of the protocol of the cross-sectional component is given elsewhere in this supplement [3]. The cross-sectional component sought to recruit and measure children between the ages of 18 and 71

TABLE 2. Complementary feeding guidelines at the Ghanaian site

<p><i>Before 6 months, give only breastmilk. Do not give any water, fruits/fruit juice or porridge</i></p> <p><i>Introduce new foods gradually by 6 months of age:</i></p> <p>The first complementary food may be cereal porridge given by spoon one or two times a day</p> <p>As the child grows, increase the amount and frequency of feeding</p> <p>Continue to breastfeed on demand</p> <p><i>Feed a variety of foods:</i></p> <p>Cereal porridge</p> <p>Enrich cereal porridge, soups, and stews with at least one of the following: milk, mashed beans, fish powder, mashed poultry or meat, groundnut paste, vegetable oil</p> <p>Fruits and vegetables</p> <p>Feed iron-rich foods such as fish, fish powder, meat, and poultry</p> <p>Give fruit or fruit juice with meals or snacks to help absorb iron in other foods</p> <p>Feed vitamin A-rich foods such as palm oil, mangoes, pawpaw, carrots, green leafy vegetables, and eggs</p> <p><i>The child's food must be well cooked, mashed, and softened</i></p> <p><i>Do not add pepper or other spices to the child's food</i></p> <p><i>Wash hands with clean water and soap before touching food or feeding the child</i></p> <p><i>The child should have his or her own bowl so that there is no competition with older children for food</i></p> <p><i>Children who refuse food should be persuaded to eat; do not force the child to eat. Do not fuss over a child who refuses to eat. Make mealtimes happy times</i></p>
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months who were similar to those enrolled in the longitudinal component. Various recruitment strategies to accomplish this aim were considered. In Accra, the most suitable strategy was recruitment from day-care centers, because most mothers enrolled in the study worked outside the home, and it was common practice among the targeted socioeconomic group to send their preschool children to crèches and nurseries.

The parents in the longitudinal study were interviewed in order to determine which day-care centers the target population chose for their children and at what age the children began to attend them. A total of 130 day-care centers were identified. Eighty of these either were used or were intended to be used by 80% of the mothers in the longitudinal study. The 80 day-care centers served about 6,000 children between the ages of 18 and 71 months who resided in the study areas. The following rates were applied to estimate the number to be screened: low socioeconomic status, 30%; twin births, 3%; gestational age < 37 weeks or ≥ 42 weeks, 5%; significant morbidity, 5%; breastfed < 3 months, 1%; enrolled in the longitudinal study, 10%; refusals, 2%; and residence out of study area, 1%. On this basis, it was estimated that 53% of the sample was potentially eligible. Following the MGRS protocol

[3], children who participated in the longitudinal study were excluded, as were their siblings. An additional criterion at this site was that eligible children must have resided in one or more of the study areas for at least the previous six months.

### Screening, enrollment, and survey logistics

Letters seeking permission to recruit subjects were sent to the 80 day-care centers. An additional 37 centers located within the study areas were added subsequently, because the first 80 provided an insufficient number of children. Consent was received from all but 1 of the 117 centers. Letters also were sent through schools to parents with children within the age group of interest (18–71 months) seeking permission for their children to participate in the study. Parents who consented provided home addresses and contact telephone numbers. Two field assistants were responsible for sending parental consent forms to, and retrieving them from, day-care centers. Follow-up interviewers made appointments with the parents for home visits, during which a screening questionnaire was completed with the parent. If no exclusion criterion was present, the subject was considered eligible; a survey questionnaire was administered, and anthropometric measurements were taken.

### Standardization, quality control, and data management activities

Several measures were put in place to ensure data quality. These have been described elsewhere in this supplement [3]. Standardized procedures to ensure accurate and precise anthropometric measurements were followed, as described in the MGRS protocol [6]. Generally, 10 newborns were recruited for the screening team's bimonthly (every two months) standardization session. The follow-up team conducted their standardization sessions with infants aged 4 to 12 months recruited at growth monitoring clinics. For the height standardization sessions, older children were recruited from nursery school. One of the two WHO-designated lead anthropometrists participated once annually in a standardization session to assess the accuracy and precision of each interviewer's measurements [6].

Bimonthly motor development standardization exercises were also held for all the interviewers assigned this function. Staff from the WHO Coordinating Centre visited the site every year to assess the team's performance and provide training as needed [7].

Team supervisors checked forms routinely for consistency and completeness of recorded responses. The forms approved by the team supervisors were forwarded to the staff in charge of quality control for a final check before data entry, verification, and valida-



tion [9]. Errors or inconsistencies detected at any of the manual or computerized quality control checks were referred to the appropriate interviewer for investigation and resolution.

Regular weekly meetings were held with the principal investigators and the team supervisors. Problems encountered by the respective teams were discussed, and decisions were made. Problems that could not be resolved locally were referred to the MGRS Coordinating Centre. The team member responsible for quality control also telephoned or visited 10% of randomly selected participants. This procedure was used to verify that visits were made as scheduled, assess rapport between interviewers and mothers, and verify the accuracy of collected data.

## Conclusions

There were numerous challenges to realization of the MGRS in Ghana. A highly committed staff was essential to the establishment of an efficient system that enabled three pairs of screening interviewers to cover all 25 hospitals and other delivery facilities daily. The logistic and training problems presented by these sites and the 117 day-care centers were formidable but solvable because of the human resources available to the project.

The underdeveloped system of physical addresses in Accra made it difficult and time-consuming to locate

study participants' homes. Despite this, the project staff persisted until each home was located. Locating fathers for measurements was also a challenge. With the help of some head teachers at day-care centers, a few fathers were measured at those facilities. Teams also made home visits on Sundays if this was the only time that fathers were available. The first lactation home visit at one week often coincided with the child's naming ceremony. This often required rescheduling visits. Some study mothers were concerned about exclusive breastfeeding up to six months when they had to resume work at four months. Such mothers were taught to express breastmilk for storage until needed, and others obtained permission to bring the infant to work.

Our site's success in implementing the MGRS protocol with the level of rigor that was required is attributable to the collaboration and support of many individuals and institutions. Among these were the University of Ghana, the Ministries of Health and Education, and the local offices and headquarters of WHO and UNICEF. Equally important was the collaboration of the participating hospitals and day-care centers, the study team's enthusiasm and commitment, and the participating mothers' perseverance. Without these contributions, the study could not have overcome the major challenges it faced. Patience, negotiation, and persuasion were required to secure the collaboration of all responsible personnel at the 25 hospitals and 117 day-care centers.

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# Implementation of the WHO Multicentre Growth Reference Study in India

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) Asian site was New Delhi, India. Its sample was drawn from 58 affluent neighborhoods in South Delhi. This community was selected to facilitate the recruitment of children who had at least one parent with 17 or more years of education, a key factor associated with unconstrained child growth in this setting. A door-to-door survey was conducted to identify pregnant women whose newborns were subsequently screened for eligibility for the longitudinal study, and children aged 18 to 71 months for the cross-sectional component of the study. A total of 111,084 households were visited over an 18-month period. Newborns were screened at birth at 73 sites. The large number of birthing facilities used by this community, the geographically extensive study area, and difficulties in securing support of pediatricians and obstetricians for the feeding recommendations of the study were among the unique challenges faced by the implementation of the MGRS protocol at this site.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, India, infant feeding practices

## Introduction

The World Health Organization (WHO) Multicentre

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

Growth Reference Study (MGRS) Asian site was New Delhi, India. Its sample was drawn from a subpopulation of selected neighborhoods in South Delhi in which relatively large groups of affluent, educated individuals reside. Data from a previous survey showed that children in this community having at least one parent with at least 17 years of education experience unconstrained growth [1]. To select the required community-based subpopulation, all 133 residential neighborhoods in South Delhi were identified. After neighborhoods with institutional residential areas, hostels, or low-income group housing had been excluded, 95 neighborhoods remained. Of these, the 58 with the highest land valuations were included [2, 3]. The survey referenced also showed that 80% of births in this population occurred in 46 hospitals or nursing homes throughout South Delhi [1]. This characteristic presented unique challenges for the site, as described below in greater detail.

## Planning phase

### Study timeline and preparatory activities

The initiation and duration of key study phases are summarized in figure 1. Preparatory activities were initiated on January 1, 2000. The first child was enrolled on April 9, 2000, and the last on October 31, 2001. The study was completed at the end of 2003.

Among the principal preparatory activities designed to facilitate study initiation and community acceptance were the recruitment of dedicated personnel for the various study activities and public relations efforts. To conduct the survey, written permission was obtained from local associations to survey the 58 neighborhoods described above. In some neighborhoods, presentations were made to groups of residents to facilitate required approvals and the collaboration of the community.

Institutional ethical approvals were obtained from the Ethics Committee of the All India Institute of Medical Sciences.

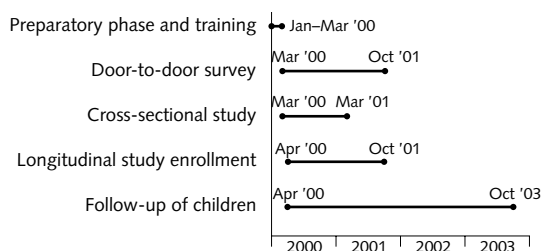


FIG. 1. Study timeline

### Study teams

The survey team, coordinated by a physician, was composed of five workers who conducted the door-to-door survey described below, and three pairs of workers who completed the cross-sectional questionnaire and took anthropometric measurements of the recruited subjects. An eight-member team, working in pairs and supervised by another physician, conducted the longitudinal follow-up. The lactation counseling team was made up of five members supervised by the overall study coordinator. A six-member data management team was also recruited and supervised by the site's data manager. The overall study coordinator conducted quality control activities and provided overall supervision of the study.

All team coordinators were physicians with training in pediatrics; the overall coordinator was an obstetrician/gynecologist. The fieldworkers were postgraduates in nutrition or social sciences. Trained lactation counselors were not available in New Delhi at the time of initiation of the study. Postgraduates in nutrition with effective interpersonal skills were therefore recruited and, together with the coordinators and physicians of the study, completed a 40-hour WHO/UNICEF breastfeeding counseling training course [4].

### Training and initial standardization

The members of the teams underwent training for various periods up to three months. The training sessions focused on applying questionnaires, the correct filling in of forms, and minimizing inter- and intraobserver variability of anthropometric and motor development measurements or observations through rigorous standardization exercises, as appropriate. Staff from the WHO Coordinating Centre and an international lead anthropometrist conducted the initial standardization session. The local team repeated standardization sessions every two months, and fieldworkers whose performance deviated from the MGRS protocol were retrained by the local lead anthropometrist. The international lead anthropometrist participated in the bimonthly sessions once a year and provided retraining as required [5].

The follow-up team members conducting the motor development assessments were trained by staff from the WHO Coordinating Centre following the motor development study protocol [6]. The site's data manager was especially trained by WHO staff to use the centrally prepared MGRS data management system described elsewhere in this supplement [7].

### Public relations

Strong community and health professional education and communication efforts were major features of the study. These were conducted in early and subsequent phases, as needed. Public awareness of the study was enhanced by posters displayed in public places, such as shops, clubs, and meeting halls in the 58 neighborhoods from which the study sample was drawn. Other informational material was distributed to local neighborhood associations, and presentations of the goals and methods of the study were made to community officials and other leaders.

A meeting was organized for pediatricians, obstetricians, and administrators of the area's major hospitals. The goals and methods of the study were presented, with the principal aims of gaining acceptance of the infant feeding recommendations of the study and building a communication network for sustaining cooperation and adherence to recommended feeding guidelines throughout and after the conclusion of the study. The network also provided a means of keeping the community and its health professionals informed of the progress of the study.

The study investigators and/or physicians visited all 73 hospitals where pregnant women recruited through the survey (described below) intended to deliver. The number of hospitals and delivery facilities was substantially larger than expected from the survey done in this community [1]. Material that was specially designed to provide information about the goals and methods of the study was distributed to administrators, pediatricians, and obstetricians and reviewed with them by study personnel.

The media were also utilized in the preparatory and subsequent phases of the study. The study received coverage in a leading daily newspaper and on a popular television news program when the first child was enrolled.

### Implementation of the longitudinal study

#### Overall strategy

A door-to-door survey was conducted in the 58 selected neighborhoods to identify pregnant women whose newborns were likely to be eligible for the longitudinal study. Children aged 18 to 71 months also were

identified by this survey for inclusion in the MGRS cross-sectional component.

All selected neighborhoods were listed alphabetically and given identification numbers (1 to 58). A computer-based random-number generator was used to determine the sequence in which neighborhoods would be surveyed. Serial numbers were assigned to the generated sequence, and the neighborhoods were surveyed in that order. All 58 neighborhoods were surveyed twice to identify 1,000 pregnant women, which was projected to be the necessary number for recruitment of the required sample size. Figure 2 summarizes the calculation of this estimate.

Exclusion criteria specific to the Indian site are shown in table 1. A total of at least 17 years of education for the mother or father was used as a criterion to select a subpopulation of infants with no constraints on physical growth, as validated in a prestudy survey conducted in the same subpopulation [1]. The morbidity criteria were selected through a consensus process among senior pediatricians of conditions most likely to affect physical growth and development significantly. The remaining exclusion criteria for individuals are

TABLE 1. Exclusion criteria specific to the Indian site

Perinatal morbidity such as severe birth asphyxia, congenital heart disease, congenital malformations, chromosomal anomalies, hormonal abnormalities, congenitally acquired infections (cytomegalovirus, toxoplasmosis, syphilis), nursery stay for more than 24 hours for morbidity
Not intending to breastfeed at all
Both parents have had less than 17 years of education

described in the methodology paper included in this supplement [8].

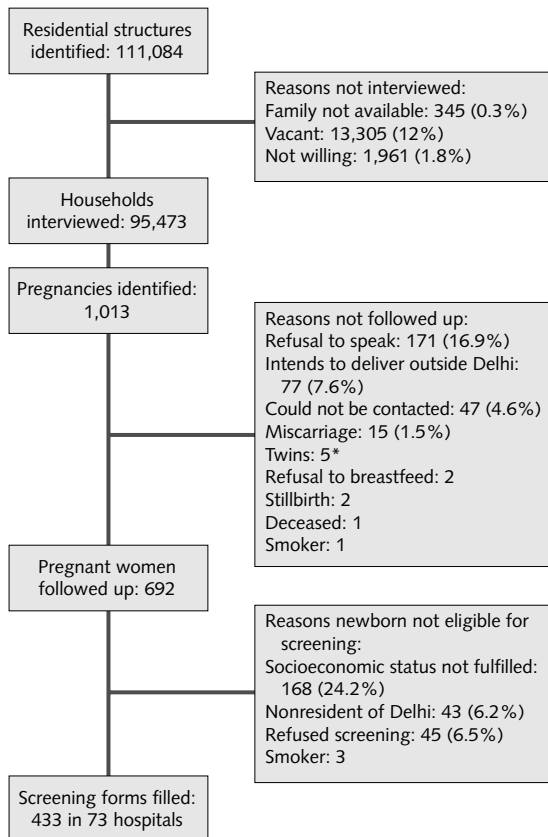
Informed consent was obtained from all pregnant women who were identified in the surveys and who agreed to participate in the study. Consenting women intending to deliver in New Delhi and fulfilling the socioeconomic eligibility criteria were revisited as appropriate at 10, 24, and 36 weeks of gestation. A study physician made the first visit, and subsequent visits were made by one of the study lactation counselors. Daily contact was maintained with all pregnant women after 36 weeks of gestation through telephone calls and/or home visits.

The intended place of delivery was ascertained at the first visit. The study coordinator contacted the hospital authorities and the subject's designated obstetrician and pediatrician. They were informed of the study and given documents relevant to its goals and methods, and permission was requested for a visit to their patients soon after delivery. The families were requested to inform the study coordinator or lactation counselor of the delivery as soon as possible. Mobile telephone numbers of study personnel were attached to the expectant mother's antenatal card to help families meet this request.

A lactation counselor visited the hospital soon after each delivery. A study physician and two members of the follow-up team visited after the initial visit of the lactation counselor. These teams were on 12-hour shifts to ensure contact with the mother as soon after delivery as possible. The follow-up team physician screened the child for eligibility and obtained oral informed consent from a parent for the infant's participation.

### Follow-up logistics

The first visit of the follow-up team was scheduled for two weeks after delivery. The child was given a gift and rescreened for eligibility at this visit. This was necessary to identify "hidden refusals" or "hidden ineligibles," e.g., infants whose fathers did not support the mother's initial decision to participate or infants whose mothers used formula soon after delivery. Written informed consent was obtained at this visit, and a baby's participation diploma was given to the mothers. Anthropometric measurements were recorded on the diploma at each visit. Hidden refusals and ineligibles



\* One woman was a smoker; she also had twins

FIG. 2. Flow chart for identification of pregnancies

were excluded. All refusals, subjects ineligible owing to breastfeeding intentions, and dropouts from the study were contacted at the child's first birthday for the 12-month study [8].

Home visits for obtaining anthropometric measurements and ascertaining feeding practices, intake of vitamin and mineral supplements, and morbidity were made according to the MGRS protocol [8]. Visits by the follow-up and lactation teams were conducted separately. If the mother inadvertently made concurrent appointments for both teams, the follow-up team waited outside the room until the lactation counselor completed her interview (fig. 3).

When the infants were four months of age, motor development assessments were initiated and repeated monthly in the first year and every two months in the second year until the child could walk independently [6].

### Lactation support and complementary feeding

Several visits by the lactation counselors were made to boost the low rates of exclusive breastfeeding characteristic of this setting [1]. These included alternate-day visits during the first week after birth and weekly visits for the first four months. Visits were made every two weeks from four to six months, and monthly visits

were made until the child's first birthday. The lactation counselors often interacted with grandmothers, because in this setting they often determine child feeding practices.

A week before the child reached the age of six months, the lactation counselor visited to provide guidance on complementary feeding. Each mother was given complementary feeding guidelines prepared by the investigators, a booklet containing nutritious and appetizing recipes, a plate and spoon, and a food calendar divided by months that permitted the caregivers to record foods consumed by the child. The complementary feeding guidelines developed by the investigators were finalized following feedback that was obtained from nutritionists and pediatricians of the major participating hospitals (table 2).

### Implementation of the cross-sectional study

Children aged 18 to 71 months were selected for the cross-sectional study from the door-to-door survey conducted primarily to identify participants for the longitudinal study. Two members of the cross-sectional team visited children recruited to this study component. If a household had a pregnant woman and one or more eligible children aged 18 to 71 months, only the

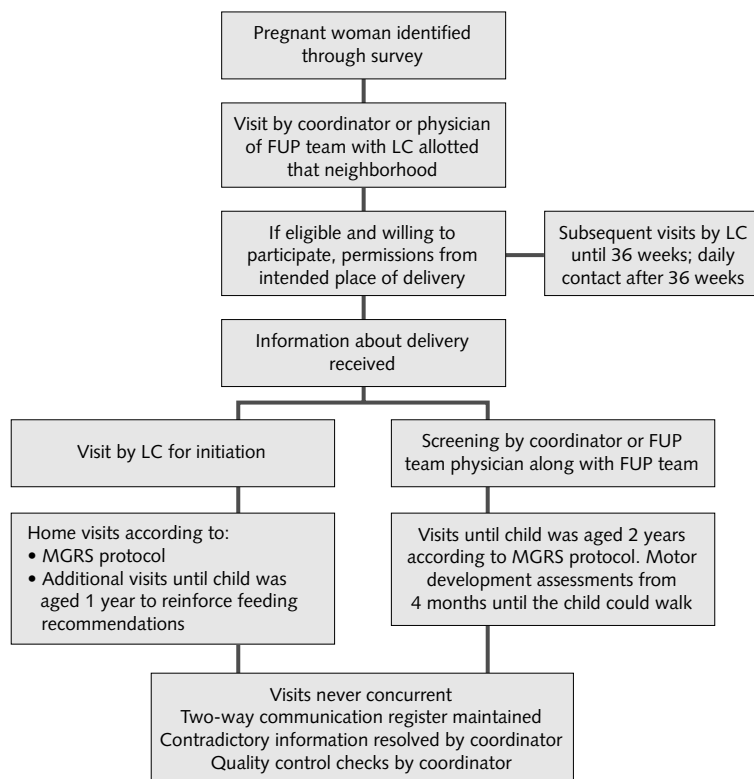


FIG. 3. Coordination between screening, follow-up (FUP) team, and lactation counselor (LC)

TABLE 2. Complementary feeding guidelines at the Indian site

Feeding practice	6–8 mo	9–11 mo	12–24 mo
Breastfeeding	Continue	Continue	Continue
Complementary foods			
Start	At 6 mo		
Quantity	280 kcal	450 kcal	750 kcal
Frequency (meals and snacks)	2–3	3–4	4–5
Consistency	Mashed, very soft	Soft	Finger foods, family diet
Food diversity	Give vitamin A-rich fruits and vegetables, meat, poultry, and fish. Use fortified foods such as iodized salt and iron-fortified flour		
Active feeding	Feed infants yourself, assist older children. Offer favorite foods if appetite is low. Talk to the child while feeding. Feed slowly and patiently. Minimize distractions. Feed from a separate bowl or plate		
Feeding during illness	Feed frequently and patiently. Give favorite foods. After recovery feed more often		
Hygiene and food handling	Wash your hands and the child's hands before feeding. Serve foods immediately after preparation. Use clean utensils to prepare and serve food. Do not use feeding bottles		
Other advice	Ensure immunization schedules are complete. Use oral rehydration therapy during diarrhea. Follow your pediatrician's recommendations for multivitamins and iron-folic acid supplements. Provide children with opportunities for exploration and autonomy		

pregnancy was followed up; if multiple eligible children 18 to 71 months were present in a household, only the youngest child in the family was included in the cross-sectional study component. The 1,490 children for the cross-sectional study were recruited successfully after surveying the first 51 neighborhoods.

## Standardization, quality control, and data management activities

### Standardization sessions

Anthropometric and motor development standardization sessions were conducted regularly for the relevant teams, as specified in the MGRS protocol [5, 6]. The anthropometry sessions were conducted every two months in one of the study clinics at an urban field site. Standardization sessions involving newborns were conducted at the All India Institute of Medical Sciences. The children assessed during the motor development standardization sessions were taken from among the participants in the longitudinal study.

### Quality control activities

Quality control checks were performed on 10% of the follow-up and lactation visits. These were fixed for the Wednesday and Saturday of each week. On these days, the coordinator listed all follow-up and lactation visits that had been made since the last quality control check and randomly selected 10% of them for follow-up. Telephone calls were made to those selected. Information

pertaining to morbidity, supplement intake, child feeding practices, maternal work, and the follow-up team's anthropometry technique and, if appropriate, lactation counseling was obtained from mothers. Feedback was obtained on the frequency and content of counselors' visits. Feedback also was obtained on any problems they faced as participants in the study. Information obtained in these quality checks was compared with information obtained by the teams. The study coordinator reviewed any inconsistencies with the relevant team.

Daily meetings were held by each of the study teams with their coordinators. Weekly review meetings were held with the project coinvestigators and each of the study teams. However, most queries and problems were resolved on a daily basis.

### Data management

Data management activities followed procedures established by the centrally developed data management system [7]. The forms filled out by the different study teams were checked manually by the respective coordinators and forwarded to the data manager within 24 hours of collection. Double data entry and validation were completed within the subsequent 48 hours. The data were transmitted to the MGRS Coordinating Centre in Geneva on a monthly basis.

## Conclusions

The implementation of the MGRS at the Indian site was a challenging task that required careful planning and

implementation. The large number of hospitals and other delivery sites used by this community precluded identifying potentially eligible infants soon after birth, as was done in all other MGRS sites. The requirement of the protocol that anthropometric measurements be obtained soon after birth made that approach impossible. Thus the door-to-door survey described above was necessary. This was particularly challenging. It meant obtaining permission to survey in each of the 58 neighborhoods and visiting 111,084 households over an 18-month period. The study area covered 116 km<sup>2</sup>. This required overcoming serious practical constraints presented by gated communities and the work and social demands on the largely professional class of participants.

Another important challenge concerned securing the support of pediatricians and obstetricians and their endorsement of the feeding recommendations central to the MGRS protocol. Few physicians in this setting are convinced that withholding prelacteal feeds and exclusive breastfeeding for six months are

relevant for families of high socioeconomic status. This barrier could not have been overcome without the public relations efforts initiated at the onset of the study and the strong international presence evident in all MGRS sites.

There were and are few well-trained lactation counselors in New Delhi. Thus the services of those trained for this study were in great demand. Although this was helpful in supporting recommended feeding practices, lactation counselors were often called upon to support both study participants and those not participating. Throughout the study, a lactation counselor was on call 24-hours a day, and a study vehicle remained with her so that visits could be made until late evening, if required. As a result of the MGRS implementation, lactation training workshops for nurses were organized at some of the major hospitals and the All India Institute of Medical Sciences on several occasions. In the end, it is gratifying that a great team effort helped overcome these multiple challenges and ensured data of high quality.

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# Implementation of the WHO Multicentre Growth Reference Study in Norway

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MRGS) European site was Oslo, Norway. Oslo has a high breastfeeding rate. Ninety-nine percent of mothers initiate breastfeeding soon after delivery, and 80% continue for at least six months. There is no evidence that socioeconomic conditions constrain growth. As in other sites, the study had two components, longitudinal and cross-sectional. Recruitment for the longitudinal component was conducted in three hospitals that account for most births in Oslo. Approximately 850 subjects were screened in one year by using a systematic allocation scheme to recruit a sample of about 300. Recruitment for the cross-sectional component was based on a systematic interval sampling scheme prepared by the National Registry. More than 4,000 subjects were screened to achieve the required sample size. One of the major challenges of the study was to achieve an acceptable participation rate; great efforts were made to motivate pregnant women via the health care system and the media.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, infant feeding practices, Norway

## Introduction

The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) European site was Oslo, Norway. The population of Oslo is about 500,000, and there are approximately 7,700 births annually [1]. The city has a high breastfeeding rate. Ninety-nine percent of women initiate breastfeeding soon after delivery, and 80% continue breastfeeding for at least six months [2]. Oslo's infant mortality rate was 3.2 per 1,000 live births in 1998 [3], and there is no evidence that socioeconomic status constrains growth in early childhood [4]. The city has an excellent breastfeeding support system and a population characterized by low geographic mobility, and it is at sea level.

As in all other sites, this study had two components, longitudinal and cross-sectional. The longitudinal component followed children from birth through 24 months. The cross-sectional component studied children aged 18 to 71 months. The sample for the longitudinal component was drawn from three hospitals that account for more than 95% of the city's births: Ullevaal, Rikshospitalet, and Aker. All three are designated as Baby-Friendly Hospitals by WHO/ UNICEF [5]. Less than 1% of women deliver their infants at home [6].

## Planning phase

### Study timeline and preparatory activities

Planning for the study began in September 1998, when a coordination center was established at the National Breastfeeding Centre in Rikshospitalet University Hospital. The timeline for the major phases of the study is summarized in figure 1.

The study was presented to the directors of the three participating hospitals, their physicians-in-chief and head midwives, and other maternity ward staff. Health personnel working in antenatal care or child health clinics were informed through meetings and written material of the goals and procedures of the

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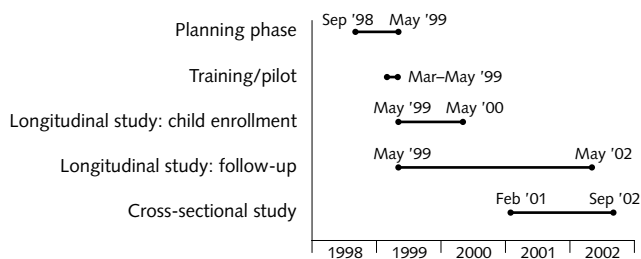


FIG. 1. Study timeline

study and their respective roles in supporting the successful implementation and completion of the study. Almost 100% of parents take their children to Oslo's public child health clinics during the children's first years of life. Cooperation agreements were therefore developed with child health clinics, and the research team sent letters outlining study procedures to the respective clinics as children from their catchment areas were enrolled.

Announcements in journals for health personnel and in the city's newspapers were used to recruit staff for the various positions in the study. Since the response was high, personnel with the best qualifications were recruited.

Institutional approvals were obtained from Rikshospitalet, Ullevaal, and Aker hospitals, the Regional Ethics Committee for Medical Research, the Data Inspectorate, and the Norwegian Board of Health.

### Study teams

The study team consisted of two principal investigators who were physicians, one project coordinator, one supervisor, five lactation counselors who had been trained as midwives or public health nurses, eight follow-up interviewers who were nurses' aides (specially trained to work with children), a data manager and two data clerks, one quality control staff member, and a study secretary.

### Training and initial standardization

The training phase lasted two months. Extensive practical anthropometric training with children of relevant ages followed a review of the underlying physiology of physical measurements and growth. The measurement techniques of the screening and follow-up teams were standardized against the measurements of one of the two WHO lead anthropometrists [7]. All candidates met the standardization criteria.

The follow-up team was trained in interview techniques and dietary assessment methods. The lactation team went through an extended training program on lactation counseling. All members of the lactation team became International Board Certified Lactation Consultants during the study period.

### Adaptation of study materials and procedures

The study materials were translated and adapted to local conditions. The questionnaires reflected exact translations of the master English version, with a few site-specific variables (e.g., indicators of socioeconomic status and site-specific complementary foods) added as required in the master Manual of Operations [8].

Child rearing practices and encouragement by training could influence the acquisition of motor development milestones [9]. As a general practice, Norwegian parents are advised by the child health clinics not to push the baby to sit in an upright position, but to wait for the child to do this spontaneously. Hands-and-knees crawling is considered an important milestone that children should not skip. If it does not occur within a certain period, parents are advised to actively stimulate its development [10]. These practices were not contradicted by the study team when implementing the motor development study protocol [11].

### Public relations activities

Achieving a high rate of participation was considered a challenge, because this community generally does not accept efforts of this type easily. Thus the assistance of the National Nutrition Council in the development and implementation of a public relations plan was particularly valuable.

Health personnel working in antenatal care were requested to display posters specially made for the study and to distribute informational leaflets to pregnant women to prepare them for a possible screening interview. All child health clinics were also sent posters introducing the study to the public.

A launching ceremony was organized with the Director-General of WHO, Dr. Gro Harlem Brundtland, as the main speaker. The event was given extensive media coverage. A proactive press strategy resulted in the publication of several articles in the main newspapers during the data collection period.

The children participating in the longitudinal study received small gifts at enrollment and on their first two birthdays, and those who completed the study were entered in a drawing in which the five winners would each receive US\$280. Every year a picnic for all participants was arranged in Oslo's main park to express the gratitude of the MGRS team and provide motivation for continued participation. Newsletters relating the progress of the study were also distributed to participants. The main factors motivating the parents to participate were probably the study team's professionalism and the global importance of the study. Both of these aspects were incorporated into all public relations activities.

## Implementation of the longitudinal study

### Sampling strategy

The screened population was selected to represent all children born in Oslo from May 1999 to May 2000. The recruitment rate at each hospital was related to the percentage of births each hospital was expected to contribute to the city's annual deliveries. An even seasonal distribution was achieved in all hospitals by frequent, regular visits to each by the study team.

Although most selection criteria were common to all sites [8], exclusion on the basis of morbidity was site-specific (table 1). In Norway the pediatric practice is not to measure the length of breech-delivered infants, because of concerns related to the risk of hip dislocation. Therefore, breech-delivered newborns were excluded at screening. Since there is no evidence for constrained growth among economically less privileged groups in Norway, socioeconomic status was not a criterion for eligibility. Regarding intention to breastfeed, no questions were asked regarding the intended duration of breastfeeding, because the rates of initiation are high, the duration is generally six months or longer,

TABLE 1. Exclusion criteria for morbidity at the Norwegian site

Criteria for assessing newborns
Serious birth asphyxia (hypoxic ischemic encephalopathy [HIE] level 2 or 3)
Seizures
Lack of muscle tone indicating possible neurological diseases
Hydrocephalus or cerebral hemorrhage
Serious infections, sepsis, meningitis, or encephalitis
Impaired respiratory function (definition: is in need of mechanical ventilation or increased oxygen requirements for more than 72 hours)
Congenital cardiovascular conditions (not atrial septal defect [ASD] or persistent ductus arteriosus [PDA])
Congenital abnormalities
Symptoms indicating chromosome abnormalities, Down syndrome, Turner syndrome, and others
Signs of having suffered from intrauterine infection
Criteria for assessing children between 18 and 71 months
Malignant disease, past or present
Chronic anemia
Chronic cardiac disease that influences daily activities
Chronic lung disease that influences daily activities
Chronic gastrointestinal, liver, or renal disease
Endocrine disorders
Chronic neurological disease that influences daily activity
Chronic mental disease that influences daily activity
Chronic systemic disease
Malformations that clearly influence daily activities and/or interfere with anthropometric measurements
Other chronic diseases that clearly influence normal daily activities

and the duration is often related to factors other than a mother's motivation to breastfeed.

Screening was carried out only on weekdays. This was not expected to result in a biased sample. Data from the 1997 Medical Birth Registry of Norway showed that 14.6% of children born at Oslo hospitals were delivered by cesarean section; 5.4% were planned cesarean sections, performed on weekdays [6]. Screening on weekdays alone thus implied a slight overrepresentation (by 2.2 percentage points) of elective cesarean section deliveries in the sampling frame. However, any bias introduced by this scheme had little if any relevance to expected child growth, so extending screening to include weekends was not considered further.

### Screening and enrollment of children

The longitudinal component required that 300 infants be enrolled [8]. Thus, based on the number of days available for screening in one year, six children were to be enrolled weekly. The available data related to the different exclusion criteria and the anticipated enrollment rate indicated that 43% of those screened would be enrolled successfully. Therefore, to enroll six children per week, 14 screening interviews were needed per week. The sampling fraction recruited from each hospital was determined by dividing the estimated number of children born during a five-day week (see above) by the 14 screening interviews needed. The first child screened was the first born after 8 am on the index recruitment day. Thereafter, sampling was performed by systematic allocation (every fourth birth). If a designated screening interview could not be carried out because of a language barrier or serious illness, the next mother on the chronological list was interviewed as a replacement. A total of about 850 mothers were screened during a 12-month period. Written informed consent was obtained from all mothers participating in the study.

### Follow-up logistics

Follow-up was carried out as outlined in the MGRS protocol [8]. The first home visit was scheduled at two weeks postpartum, during which baseline data were collected and eligibility and consent were reassessed. Mothers who indicated that they smoked or were already giving formula to their infants on a regular basis were considered "hidden ineligible" and excluded from further participation, in accordance with the MGRS protocol. Mothers who initially agreed to participate but were no longer interested by day 14 were considered "hidden refusals." Hidden ineligibles and refusals, as well as children who dropped out of the study before the age of 12 months, were contacted a few weeks before the child's first birthday for participation in the 12-month study [8]. The procedure was to call

at least five times at different times of the day over a two-week period. If no contact was achieved by then, the family was defined as “not traceable.”

The motor development assessments [11] were initiated in April 2000, about 10 months after screening was initiated, which meant that the initial milestones could not be assessed for some infants.

### Lactation support and complementary feeding

A combined screening and lactation team was established. Soon after enrollment, the lactation counselors helped newly delivered mothers in the maternity ward with the initiation of breastfeeding. The same consultant followed the mother–infant pair until the child’s first birthday to provide frequent and individual lactation support. The mothers were contacted by telephone and lactation was assessed the day following discharge from the hospital, usually two to four days postpartum. Close follow-up of breastfeeding problems was offered from their onset. In addition to four scheduled home visits at weeks 1 and 2 and months 3 and 6, lactation counselors kept in contact with mothers by telephone at least once per month. Mothers having breastfeeding problems received extra support until the problems were resolved. A hotline for emergency support was available seven days a week from 8 am to 8 pm.

The mothers were advised to introduce complementary foods to their infants by six months. The infant nutrition guidelines developed by the Norwegian National Nutrition Council [12] were followed (table 2). The council’s feeding guidelines are based on Norway’s dietary patterns, which include cereals and potatoes as important staples. Cod liver oil is recommended from the age of four weeks as a vitamin D and essential polyunsaturated fatty acid supplement. In addition to the prevention of vitamin D deficiency, sufficient iron intake is a concern. Iron-fortified porridge is recommended most commonly to ensure that the infant’s iron needs are met. Water rather than sweetened beverages is recommended, since consumption of the latter tends to replace more nutrient-dense diets.

## Implementation of the cross-sectional study

### Sampling strategy

The number of children aged 18 to 71 months living in Oslo during the implementation of the cross-sectional component of the study was estimated to be 28,000 [1]. From this population, 1,260 children were to be selected for the cross-sectional study. The sampling was done in cooperation with Statistics Norway [13]. All persons living on a permanent basis in Norway are registered in the National Registry. Information

TABLE 2. Complementary feeding guidelines at the Norwegian site

<p>From the age of four weeks, 10 µg of vitamin D is recommended, preferably through cod liver oil</p> <p>If the baby needs a supplement to breastmilk, iron-fortified infant formula is recommended for the first 12 months</p> <p>Complementary foods should be gradually introduced from the age of four to six months, while the baby is still breastfed, giving small amounts of only one type of food for some days so that possible reactions can be detected. This recommendation was revised in 2002, and exclusive breastfeeding for the first six months of life is now recommended</p> <p>Introduction of complementary foods may start with pureed potatoes, vegetables, fruits, and/or porridge</p> <p>After the introductory phase, pureed fish and meat, together with the staple potato and vegetables (dinner) should be introduced</p> <p>Do not add salt to baby food</p> <p>Iron-fortified baby cereals are a good source of iron. Two meals per day will ensure an adequate intake. If the child receives other good sources of iron such as dinner with meat, one may also use home-prepared porridges based on oatmeal, for example</p> <p>If the child has a history of food allergy, eggs, fish, and peas should not be introduced until the child is one year old</p> <p>Offer the child water instead of squash</p> <p>From the age of one year, children should receive the family food without too much salt</p>
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on each registrant includes an identity number and the name and address of the mother and father. The registry is updated every third week. By combining files from the National Registry and the Medical Birth Registry, it was possible to select only children both born and living in Oslo, to eliminate twins, and to select only one child per family. Based on population characteristics and experience from the longitudinal study, a participation rate of 31% was anticipated. According to the experience of Statistics Norway, it was necessary to increase the sample size by about 20% to allow for factors such as families not responding to telephone solicitations. A total of 5,185 children were sampled for the screening interview.

The sample to be screened was selected by a systematic interval sampling scheme. All children in the targeted age groups were sorted according to age and their home’s postal code. A random entry point of sampling was selected, and then sampling was carried out at a fixed interval. This method results in a randomly selected, representative sample of designated age cohorts and provides a representative geographic distribution.

The sampling was divided into four periods to enable better focus on specified age groups. This method provided the most up-to-date lists possible and included fewer families who had left Oslo.

### Screening, enrollment, and survey logistics

A letter explaining the goals and procedures of the study was sent to mothers of potentially eligible children one to two weeks before a projected screening interview. These letters were followed by telephone calls. Mothers were called at least five times at different times of the day over a two-week period. If no contact was achieved after the fifth attempt, the family was defined as "not traceable." Appointments for the cross-sectional survey interview and measurements were made with subjects who were eligible and willing to participate. Most visits occurred in the evenings in the subjects' homes to accommodate parents working outside the home.

### Standardization, quality control, and data management activities

All quality control procedures outlined in the MGRS protocol were implemented [8]. Every questionnaire was checked, and irregularities were resolved in consultation with the appropriate interviewer. Ten percent of mothers (randomly selected) were called by telephone to review previous responses to interview questions, validate that visits were done, and assess the content of the visits.

Data management procedures were implemented by using the MGRS data management system, and the data management procedures of the study, described elsewhere in this supplement [14], were adhered to. The interviewers were given an overview of the data management system and brief hands-on experience with data entry. This provided a more complete understanding of the data management procedures

and emphasized the importance of completing questionnaires accurately.

### Conclusions

The MGRS was a demanding study, and several major challenges had to be overcome to bring it to a successful completion in Norway. Chief among these in the longitudinal component of the study was the need to maintain a high level of momentum for continued participation in 21 follow-up visits over a two-year period. Because both parents of most young families work outside the home, maintaining commitment over a two-year period was a major achievement for the families and the study team. The behavioral and technical skills of the follow-up team were crucial to achieving high rates of continued participation, and more than 85% of the enrolled sample completed the 21 visits. The main reason for dropping out was the family's leaving Oslo.

The bimonthly (every two months) anthropometric standardization sessions were also a very demanding aspect of the longitudinal component of the study. Nonetheless, their necessity was also evident [7]. The difficulties presented by these sessions are clear from the fact that a 40% overrecruitment rate was necessary to ensure that a sufficient number of parents and children participated in any single session. Most children appeared to find the sessions stressful.

Despite these and other challenges, parents and staff sustained their participation because of the important role that growth standards play in developing and developed countries. Most participants viewed their participation as meeting a larger public service responsibility to Norway's and the world's children.

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# Implementation of the WHO Multicentre Growth Reference Study in Oman

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Study (MGRS) Middle East site was Muscat, Oman. A survey in Muscat found that children in households with monthly incomes of at least 800 Omani Rials and at least four years of maternal education experienced unconstrained growth. The longitudinal study sample was recruited from two hospitals that account for over 90% of the city's births; the cross-sectional sample was drawn from the national Child Health Register. Residents of all districts in Muscat within the catchment area of the two hospitals were included except Quriyat, a remote district of the governorate. Among the particular challenges of the site were relatively high refusal rates, difficulty in securing adherence to the protocol's feeding recommendations, locating children selected for the cross-sectional component of the study, and securing the cooperation of the children's fathers. These and other challenges were overcome through specific team building and public relations activities that permitted the successful implementation of the MGRS protocol.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, infant feeding practices, Oman

## Introduction

The Middle East site of the World Health Organization (WHO) Multicentre Growth Reference Study (MGRS)

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

was the capital city of the Sultanate of Oman, Muscat. Oman is located at the southeastern corner of the Arabian Peninsula. The city overlooks the Arabian Sea and the Persian Gulf. Its population resides at altitudes close to sea level. Of the country's 2.5 million inhabitants, more than a quarter reside in the capital area. About half of the resident population in Muscat (55%) is Omani [1], the remainder being expatriates. Muscat's population is relatively affluent and has ready access to highly developed preventive and curative health services.

Ninety-six percent of births in Muscat take place in two hospitals: Royal (4,969 births in 2001) and Khoula (3,548 births in 2001) hospitals [1]. These births include high-risk pregnancies that are referred from outside the capital area. Both hospitals serve a clearly defined catchment area that includes most of the women resident in Muscat. All communities within the catchment area were included in the study except Quriyat, a remote district of the Governorate.

A survey was conducted to identify socioeconomic, demographic, and behavioral characteristics of the subpopulation within Muscat whose children's linear growth is unconstrained by social and other environmental conditions [2]. The mothers of 336 children aged 28 to 43 months were selected from the national Child Health Register and interviewed. The children's weights and heights, the maternal height, child feeding practices, and the families' socioeconomic status were assessed. The participants' potential willingness to participate in the MGRS was also ascertained. The survey had a refusal rate of 0.1% [2]. The survey results demonstrated that more than 20% of those interviewed were able to follow MGRS feeding recommendations. The survey also identified specific socioeconomic status indicator cutoffs of families whose children experience unconstrained growth in early childhood. These were a monthly household income of at least 800 Omani Rials (US\$2,083) and at least four years of maternal education. Mobility was low, but some families (39%) usually traveled out of Muscat on vacation for short periods during the summer months.

## Planning phase

### Study timeline and preparatory activities

The initiation and duration of the key phases of the study are summarized in figure 1. Approval to recruit from the two participating hospitals was obtained from the Directors General of the Royal Hospital and Muscat Region (for Khoula Hospital). Members of the research team met with the chief nurses and the heads of the maternal and pediatric units of each hospital to explain the aims and procedures of the study and their respective roles in its successful implementation, especially in facilitating subject recruitment and the breastfeeding of newborns.

### Study teams

The study group was composed of three field teams—the screening, follow-up, and lactation support teams—with their respective supervisors and quality control staff. The data management team based at the local coordination center was supervised by the site data manager and his assistant. The coordination team was made up of the site's principal investigator, a research associate, the supervisors and quality control staff of the three field teams, the data manager and assistant, a pediatric consultant, and a breastfeeding adviser. The field teams were formed for functions defined by the longitudinal study, but two of them implemented the cross-sectional study: the lactation team to screen and the follow-up team to interview recruited subjects and take anthropometric measurements. When the cross-sectional component began, lactation counseling activities were nearly completed, and the volume of longitudinal follow-up visits was low enough to accommodate the additional visits. The supervisors and quality control staff members fulfilled their functions in positions determined by local needs at different stages of the implementation of the study. The pediatric consultant defined the neonatal morbid-

ity exclusion criteria and held meetings with the pediatricians of the two hospitals to secure their support for the implementation of the study. The Muscat Region Director General provided key logistic and personnel support for the implementation of the study.

Six nutritionists were recruited to the screening team. This group worked in pairs and rotated between the hospitals. An International Board Certified Lactation Consultant trained nine nurses from the maternal and pediatric wards of the two hospitals, four of whom were recruited as lactation counselors for the study. Each counselor was assigned to specific residential areas. Eleven nurses and dietitians were recruited to form five working pairs of the follow-up team. One member of each pair was assigned permanently to a specific residential area, and the other six were rotated every two months. Three part-time data entry clerks worked on the data management team, and three part-time study secretaries were responsible for day-to-day administration and coordination functions (fig. 2).

### Training and initial standardization of study teams

The longitudinal screening and follow-up teams were trained to make anthropometric measurements by a member of the MGRS Coordinating Centre and standardized against the WHO lead anthropometrist before the start of data collection. All interviewer teams were trained to administer oral interviews and complete questionnaire forms with the aid of the interviewer guides. Six members of the follow-up team were trained to perform motor development assessments. In addition to the overall administration of the project, the secretaries were trained to coordinate the day-to-day activities of the various teams and to maintain study registers and participation flux charts.

### Adaptation of study materials and procedures

The MGRS Manual of Operations was adapted to the Omani context, and all questionnaires were translated

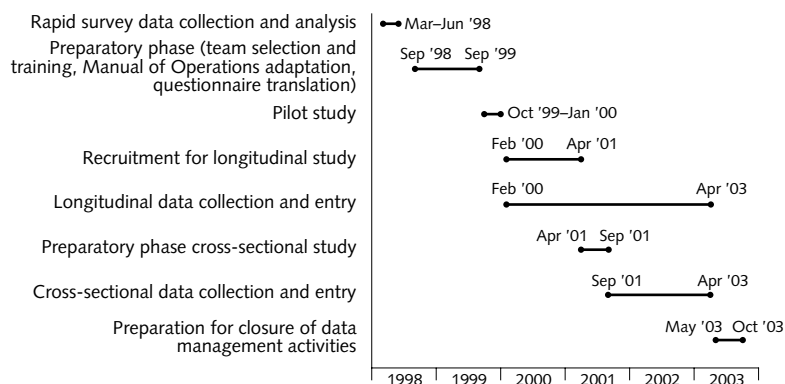


FIG. 1. Study timeline

into Arabic and back-translated into English at WHO headquarters in Geneva [3]. The interviewer guides were also translated into Arabic. Gender segregation is the norm in Oman. Thus, the availability of men during home visits was often low, and the fieldworkers, all of them female, were often not permitted to take their measurements. Therefore, two men were trained to measure adult weight and height, and the fathers had the option of coming to the local coordination center or were visited at work or at the health center nearest their home for these measurements to be taken.

### Public relations activities

Media coverage, mostly by newspapers and radio, was secured when the study was launched and in the initial phases of the cross-sectional component. Despite these efforts, the study experienced a high refusal rate. To address this problem, the public relations officer in one of the hospitals assisted the longitudinal screening team by meeting with fathers during afternoon visiting hours and encouraging them to participate. Occasionally a male member of the coordination team would also talk with a reluctant father about the importance of taking part in the study.

A booklet explaining the importance of breastfeeding and offering practical advice on how to do it successfully, an informational leaflet describing the aims and

procedures of the study, and letters requesting fathers' and employers' collaboration were distributed. A study newsletter in Arabic was also distributed to all families recruited in the longitudinal component. Another newsletter in English was published for hospital and health clinic staff and other key supporters.

Two receptions were held for the longitudinal study participants at which gifts were given to all the children and their mothers. This was done to maintain the group's morale and thank the participants for their commitment to the study. Discount cards to shops and eateries were also provided, and the coordination team helped arrange doctor's appointments for enrolled children when required. MGRS seals also were placed on the children's health cards. This accorded them priority status at health centers. The mothers also were given tokens of appreciation at the end of the two-year follow-up.

## Implementation of the longitudinal study

### Sampling strategy

The recruitment target was set at 6 to 8 babies per week in order to enroll 312 children over 12 consecutive months. High ineligibility and refusal rates in the pilot phases of the study demonstrated the need to screen

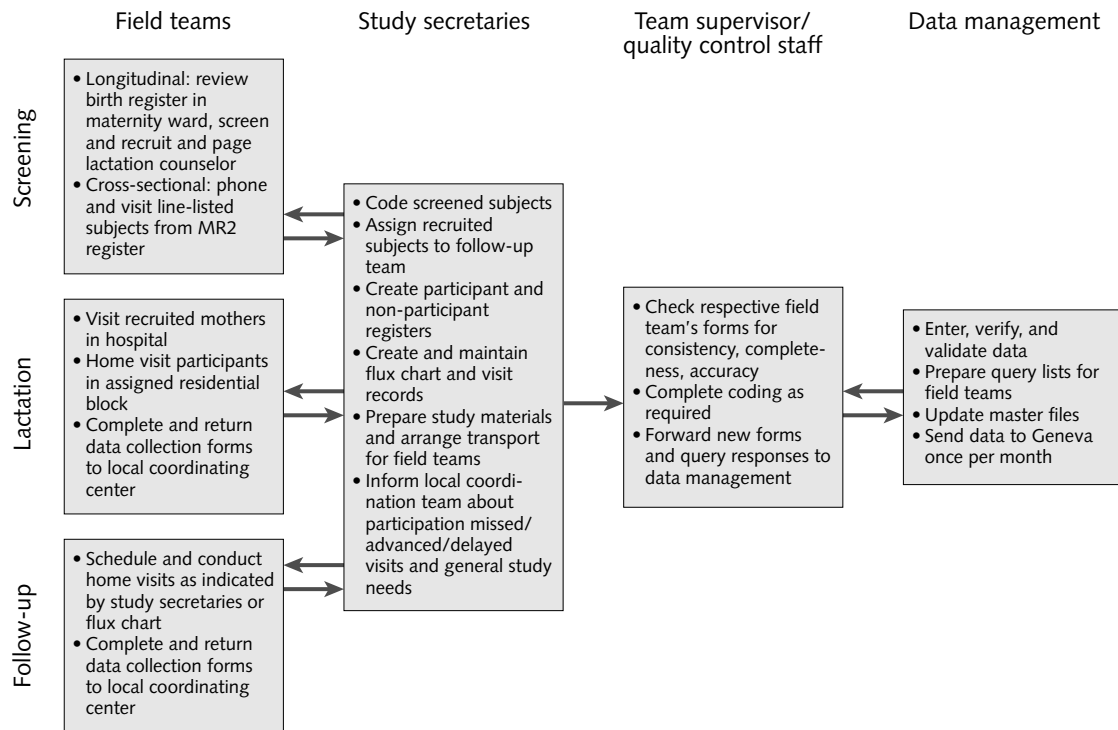


FIG. 2. Team coordination flow chart



all births in order to meet the sample size target. A weekly enrollment ratio of 4:3 from the Royal and Khoula hospitals was decided on to reflect the number of births in each hospital.

### Screening and enrollment

Screening was done twice daily in each hospital, at 8 am and 8 pm Saturday through Wednesday. All children born in the previous 12 hours were screened. Screening stopped at each hospital when that hospital's weekly quota was met, but the quota was sometimes exceeded to compensate for recruitment shortfalls in previous weeks. All babies admitted to the Special Care Baby Unit for more than 24 hours were excluded, unless the unit's attending physician indicated that the infant's diagnosis would not affect growth adversely. The perinatal morbidity exclusion criteria are summarized in table 1. Only oral consent was obtained at screening in most cases because of the disinclination in most families to give written consent.

### Follow-up logistics

The enrolled subjects were listed in the study register at the local coordination center and assigned for follow-up to the team responsible for their residential area. Each mother was followed throughout the study by one nonrotating member of the follow-up team to provide stability. Motor development assessment was done from the age of five months by members of the follow-up team on the same schedule as the follow-up visits.

### Lactation support and complementary feeding

The lactation counselors visited the enrolled mothers within 24 hours of delivery to ensure successful initiation of breastfeeding and reconfirm the mothers' willingness to participate. They maintained a 24-hour

hotline, seven days a week, to respond to acute breastfeeding problems and answer the mothers' questions and concerns. The lactation team supervisor assisted with difficult lactation problems and periodically made home visits to support the mothers, foster compliance with breastfeeding guidelines, and enhance the mothers' confidence in the study team. The MGRS in Oman adopted the complementary feeding guidelines developed by the Ministry of Health. A booklet containing these guidelines was distributed at the five-month visit (table 2).

A list of eligible families who refused to participate, were unwilling to follow the MGRS breastfeeding requirements, or dropped out of the study while the child was an infant was generated for follow-up at the child's first birthday. A random sample of 72 was selected and visited by the follow-up team to obtain anthropometric measurements, as outlined in the MGRS protocol [3].

## Implementation of the cross-sectional study

### Sampling strategy

The sample for the cross-sectional study was drawn from Child Health (MR2) registers in the 12 health centers that serve the population in Muscat. Investigations done in preparation for this study component established that 93% of the children born in the Royal and Khoula hospitals were included in the MR2 register at any 1 of the 12 health centers. The preparatory investigations also tested the ability of the MR2 registers to provide a random sample of children aged 18 to 71 months similar to that recruited for the longitudinal component of the study. Only 72% of a sample drawn from the 1995 and 1998 MR2 registers could be traced, and nearly 75% of the families had more than one child in the age range required (both nuclear and joint families). Additional resources were required to increase the contact rate so as to screen at least 80% of the target population, and the latter finding revealed the need to expand the sampling frame, since only one child per household would be eligible for the study.

After multiple births and births to expatriates had been excluded, a master list of 24,000 children aged 18 to 71 months was drawn from the 12 MR2 registers. The eligibility and consent rates observed in the preparatory phase of the study indicated that 8,000 children should be screened to recruit the required number (1,400), and therefore a random sample of 8,000 from the master list was selected for contact.

### Screening, enrollment, and survey logistics

The mothers were contacted initially by telephone to ascertain the presence of a potentially eligible child.

TABLE 1. Local exclusion criteria for the Omani site

Term	Definition
Perinatal morbidity	Admitted to Special Care Baby Unit for more than 24 hours, or information on the infant diagnosis sheet completed by attending physician identified a disease affecting growth
Intention to breastfeed	Mother unwilling to try to breastfeed for at least four months
Socioeconomic status	Household income less than 800 Omani Rials (0.384 OR = US\$1) or maternal education less than four years

The child had to be within the targeted age range, to have been breastfed for at least three months, to meet the residency requirements, and to have an Arabic-speaking mother. Consenting eligible families were visited in their homes to complete the full screening interview. When the telephone number was out of service or the call went unanswered, the family was sought at the physical address indicated in the MR2 register. The four members of the screening team each covered the same residential areas assigned to them for lactation counseling in the longitudinal component. Several efforts were set up to maximize the contact rate for screening. One team member was employed full-time to obtain additional contact information on subjects who could not be contacted by telephone or at the listed home address. Computerized registers maintained in the 12 health centers and in the city's principal obstetrics/gynecology clinic, where all women in their third pregnancy trimester are attended to, were reviewed. Health educators from each of the health centers, voluntary support groups, and the areas' wali or sheikhs also assisted in locating those who could not be contacted. These collaborative efforts were key to achieving an 80% contact rate. Two staff members were added a few months into the data collection period to assist with recruitment. At the local coordination center, the recruited subjects were assigned to the follow-up team working in their residential blocks for the home visit. The follow-up team visited each household once to administer the cross-sectional survey interview and take anthropometric measurements.

### Standardization, quality control, and data management activities

Throughout the data collection phase, the anthropometry and motor development teams participated in bimonthly (every two months) standardization sessions and received remedial training if their performance deviated from MGRS norms. The anthropometry standardization sessions of the screening team were conducted in the Royal Hospital maternity ward, and the follow-up team standardization sessions for both anthropometry and motor development were held in the Bowshar polyclinic. The children who participated in the standardization sessions of the follow-up team were recruited from well-baby clinics and from participants in the longitudinal component of the study. Standardization procedures are described elsewhere in this supplement [4, 5].

Quality control activities were also carried out as described in the MGRS protocol and Manual of Operations [3]. Telephone calls were made following all cross-sectional component screening visits, and the team supervisor made random repeat home visits to validate information that had been obtained by the fieldwork-

TABLE 2. Ministry of Health Complementary Feeding Guidelines, Oman site

<p><i>Continue frequent, on-demand breastfeeding, including night feeding for infants up to the 24th month</i></p> <p><i>Introduce complementary foods between the beginning of the 5th month and the end of the 6th month</i></p> <p><i>Increase food quantity as the child gets older:</i></p> <p>Provide infants 5–8 months old approximately 280 kcal per day from complementary foods</p> <p>Provide infants 9–11 months old approximately 450 kcal per day from complementary foods</p> <p>Provide children 12–24 months old approximately 750 kcal per day from complementary foods</p> <p><i>Increase feeding frequency as the child gets older, using a combination of meals and snacks:</i></p> <p>Feed infants 5–8 months old complementary foods 2–3 times per day</p> <p>Feed infants 9–11 months old complementary foods 3–4 times per day</p> <p>Feed children 12–24 months old complementary foods 4–5 times per day</p> <p><i>Gradually increase food consistency and variety as the infant becomes older, adapting the diet to the infant's requirements and abilities:</i></p> <p>Feed mashed and semisolid foods, softened with breastmilk, if possible beginning around 5 months of age</p> <p>Feed energy-dense combinations of soft foods to infants 5–11 months old</p> <p>Introduce finger foods (snacks that can be eaten by children alone) beginning around 8 months of age</p> <p>Make the transition to family food at about 12 months of age</p> <p><i>Diversify the diet to improve quality and micronutrient intake:</i></p> <p>Feed a high-protein diet such as meat, fish, or poultry, or legumes such as lentils, beans, peas, chickpeas, or yogurt daily</p> <p>Feed vitamin A-rich fruits and vegetables daily</p> <p>Use only iodized salt</p> <p><i>Practice active feeding:</i></p> <p>Feed infants directly and assist older children when they feed themselves</p> <p>Give each child a plate and a spoon, and encourage him or her to stay at the table during the mealtime</p> <p>Offer favorite foods and encourage children to eat when they lose interest or have depressed appetite</p> <p>Start new foods one at a time, and allow 4–7 days to observe for any possible food intolerance</p> <p>Include eggs and honey in the diet only after the child completes 12 months of age</p> <p>Do not offer more than two small coffee cups of juice per day, especially before meals, as it could decrease appetite</p> <p>Feed slowly and patiently and minimize distractions during meals</p> <p>Make mealtime a happy, pleasant time. Do not force the child to eat certain foods or finish everything on the plate</p> <p><i>Practice frequent and active feeding during illness:</i></p> <p>During illness increase fluid intake by more frequent breastfeeding and patiently encourage children to eat favorite foods</p> <p>After illness, breastfeed and give foods more than usual and encourage children to eat more food at each sitting</p>
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ers. Data forms were checked for completeness and consistency by the interviewer and her team supervisor before being submitted for data entry. In keeping with the MGRS protocol, data were entered twice and validated by centrally prepared routines before being incorporated into the study master files [6].

## Conclusions

The successful conclusion of the study required the overcoming of several particularly difficult challenges: a relatively high refusal rate, obtaining fathers' anthropometric measurements, securing the family's adherence to the feeding guidelines of the study, and locating families for the cross-sectional component of the study.

Of those eligible at screening, nearly a quarter refused to participate. In addition, almost a third of the mothers enrolled in the hospital for the longitudinal study rescinded their consent when contacted at home. This high refusal rate probably reflects the high value placed on privacy in Oman. In many cases, families were very hesitant to have people interview them at home, particularly when it involved the long-term commitment of two years. Often it was the child's father who refused consent after the mother had agreed to participate.

Participating fathers were requested to be available for at least one of the follow-up visits, but this often proved difficult and required making the adjustments

described earlier. Even when they were available, some fathers would not have their measurements taken by women, a fact that increased the logistic complexity and resource costs of the study.

Adherence to the protocol's feeding recommendations was difficult for mothers working outside the home. This was common in the professional class targeted by the study. Employers were contacted and requested to support working mothers to breastfeed their infants exclusively, e.g., by granting enrolled mothers compensated time off during the day. The large households common in Oman also proved challenging, because many individuals participate in child care. It was important, therefore, to counsel both the mother and other key family members.

Locating children selected for screening for the cross-sectional component of the study proved especially difficult. Many children on the master list, especially older ones, were no longer available at the addresses provided by the Child Health Register. Extensive efforts were required to locate these children. Even after telephone contact was established, missed appointments were common and locating potential subjects' homes was often difficult. Muscat is experiencing rapid growth that has resulted in a network of unpaved roads in both new and older neighborhoods.

However, the study was successfully implemented, thanks to the collaboration of many individuals and institutions and the tenacity of the field and coordination teams.

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# Implementation of the WHO Multicentre Growth Reference Study in the United States

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) North American site was Davis, California. For the longitudinal cohort (0–24 months), 208 infants were enrolled between January and December 1999 from five area hospitals at which nearly all Davis women give birth. The target sample size was lower in the United States than in the other sites, because recruitment in the United States was restricted to mothers who were willing to exclusively breastfeed for at least 4 months and continue breastfeeding for at least 12 months. For the cross-sectional component, a mixed-longitudinal design was used, which required approximately 500 subjects. The subjects were recruited by going door-to-door, with the sampling scheme based on the distribution of the subjects of the longitudinal study within the city. The cross-sectional sample was recruited between January and July 2001. Major challenges during implementation were maintaining daily communication with hospital personnel and scheduling home visits.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, infant feeding practices, United States

## Introduction

The World Health Organization (WHO) Multicentre

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Members of the WHO Multicentre Growth Reference Study Group and Acknowledgments are listed at the end of the first paper in this supplement (pp. S13–S14).

Growth Reference Study (MGRS) North American site was Davis, California, in the United States. Davis is a university town. Its average educational level is high. More than 95% of mothers initiate breastfeeding, and support services for breastfeeding are available. The altitude is about 15 m. The mobility of the student population is high, but for the longitudinal study, only mothers who planned to remain in Davis for at least 24 months were included. Five hospitals collectively account for more than 95% of all births to women residing in Davis: Sutter Davis Hospital, Woodland Memorial Hospital, and three hospitals in Sacramento, California—the University of California at Davis (UC Davis) Medical Center and two Kaiser Permanente hospitals. Prior to initiating this study, the research team had had extensive experience with studies on infant nutrition and growth in the community. Thus, the study site fulfilled the criteria for inclusion in the MGRS described elsewhere in this supplement [1].

## Planning phase

### Study timeline and preparatory activities

The timeline of the study is summarized in figure 1. During the first two months, the study team met with representatives from the five hospitals listed above and arranged for letters to be sent to potential subjects when they registered to give birth at each hospital. Permission to recruit newborns from the hospitals and conduct specific activities was obtained from the administrators of the hospitals. Letters to the patients described the study and indicated that study personnel would visit the mothers in the hospital shortly after delivery. Members of the study team met with the physicians in charge of each hospital's maternity ward and other relevant hospital personnel to explain the logistics of the study, introduce team members, and discuss study procedures. Letters introducing the study and explaining its logistics were sent to local physicians. During the longitudinal recruitment phase of the study,

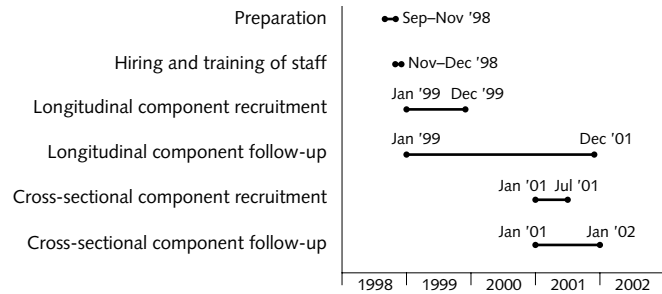


FIG. 1. Study timeline

letters were mailed to the physicians of enrolled subjects explaining the study and describing the lactation counseling services of the study.

Institutional ethical approval was obtained from the University of California Human Subjects Review Committee and the Kaiser Permanente Northern California Health Services Institutional Review Board.

### Study teams

There were three study teams for the longitudinal study: the coordination, neonatal, and follow-up teams. The coordination team consisted of the site's principal investigator, three supervisors, a study secretary, and two data entry clerks. This team had the general responsibility of overseeing all study activities. Two supervisors were International Board Certified Lactation Consultants (IBCLCs). These supervisors jointly managed the neonatal team, and one of them also served as the data manager. The third supervisor was in charge of anthropometric training and supervised the follow-up team. All three supervisors served as backup data collectors for the neonatal and follow-up teams. The neonatal team, composed of two IBCLC lactation counselors and two research assistants, was responsible for screening, lactation counseling, and data collection through day 14 of each subject's participation. The follow-up team was responsible for data collection from 1 to 24 months. They referred mothers to the lactation counselors of the neonatal team as needed. This team consisted of four research assistants.

There were two teams for the cross-sectional study: one for recruitment and a second for obtaining anthropometric measurements. The recruitment team was responsible for going door-to-door to screen and enroll subjects. This team consisted of five individuals, most of whom worked part-time. The measurement team subsequently contacted each family to complete the cross-sectional visit and take the anthropometric measurements. The team consisted of three research assistants.

All members of the data collection teams had at least a four-year college degree in a related field and qualifications consistent with the duties they would perform.

### Training and initial standardization

The study teams received training in accordance with the MGRS Manual of Operations. The breastfeeding observation protocol was standardized among the lactation counselors and the two IBCLC supervisors. The follow-up team was given instructions on the referral system to be used for women experiencing breastfeeding problems. The cross-sectional study recruitment personnel received instructions on the neighborhood recruitment scheme and the screening protocol.

### Adaptation of study materials and procedures

The Manual of Operations was adapted to reflect the team configuration implemented at this site. A home visit was added on day 3 postpartum to optimize the successful establishment of breastfeeding, in accordance with the recommendations of the American Academy of Pediatrics [2].

Minor adaptations were made to the baseline and follow-up questionnaires. Several questions were added to document socioeconomic status. In recording educational status, the number of years of higher education was "capped" at a predetermined maximum, depending on the degree obtained. The list of potential responses to selected questions was expanded (e.g., site-specific foods for the food frequency and dietary recall questions).

### Public relations activities

Study displays and informational brochures were placed in clinics and offices of physicians likely to have patients interested in the study. Study personnel visited local childbirth classes and mothers' support groups to introduce and explain the aims and procedures of the study.

The Davis, Sacramento, and UC Davis newspapers published several articles with photographs about the study, and two television segments publicizing the study were aired on local channels. The mothers and infants received a matching set of T-shirts with the local study logo as a means of thanking the participants, publicly acknowledging their participation, and

introducing the study to the wider community. Local merchants were also solicited to offer discounts and gift certificates to subjects as a means of encouraging wider community involvement.

The cross-sectional study was publicized in the local newspaper prior to the commencement of recruitment. Pediatricians were contacted and asked to encourage their patients to participate in the study. Flyers to parents were distributed through local day-care centers and kindergarten classes. A publicity table also was set up at the Davis Farmer's Market.

## Implementation of the longitudinal study

### Sampling strategy

All infants born during the enrollment period to mothers who planned to remain in Davis for at least 24 months were potentially eligible for the longitudinal study. Most subjects (95%) were recruited from the five hospitals listed above. Each of these hospitals was contacted daily, seven days a week, to identify potential subjects. Potential subjects were visited in the hospital within 24 hours of delivery by a member of the research team. Mothers who resided in Davis and gave birth at home or at other hospitals were also eligible to participate if the research team was notified and the mother could be reached within 24 hours after delivery. Women who planned to have a home birth were contacted prenatally via the designated midwife.

Eligibility criteria specific to the US site are shown in table 1. The target sample size for the longitudinal study at the US site was 200 (as compared with 300 in the other sites). The sample size was judged adequate based on the documented research experience in this community. This experience indicated that the desired final sample size (at least 70 infants) could be attained if recruitment was restricted to mothers who were willing to breastfeed exclusively for at least 4 months and continue breastfeeding for at least 12 months.

TABLE 1. Longitudinal study selection criteria specific to the USA site

Davis resident: mailing address in Davis or El Macero (a subdivision of Davis)
Perinatal morbidity: any condition that was serious enough for the infant to be kept in the intensive care unit for more than 24 hours led to exclusion. This included conditions such as respiratory illnesses, congenital malformations, maternal drug abuse, Down syndrome, and nervous system disorders
Intention to breastfeed: mother was willing to exclusively breastfeed for at least 4 months and continue breastfeeding for at least 12 months
Socioeconomic status: telephone in the home

### Screening and enrollment of children

Informed written consent was obtained from the mother after eligibility was established. If she was unwilling or ineligible, or wanted to discuss her participation in the study with her partner, written consent was obtained for the neonatal measurements only. All newborns of interviewed mothers were measured if consent for those measurements was obtained, irrespective of enrollment in the full study. Eligible mothers wishing to postpone their decision kept the consent form until the first follow-up visit at home.

### Follow-up logistics

Subjects were given the option of having home visits or going to the site's central facility. The majority preferred home visits. The neonatal team conducted home visits on days 3, 7, and 14 and at week 4 to all mothers who experienced breastfeeding problems on day 14. This allowed the lactation counselor to evaluate whether breastfeeding problems had been resolved and offer further assistance if needed. In cases where such follow-up was required, the neonatal team continued to follow the subject until week 4. Otherwise, the follow-up team initiated follow-up after the day 14 visit and conducted all home visits from four weeks to 24 months. Whenever mothers experienced breastfeeding problems after four weeks, the follow-up team contacted the neonatal team supervisor to arrange for lactation counseling. Figure 2 illustrates coordination among the teams.

The motor development assessment began at four months, according to the MGRS protocol described elsewhere in this supplement [3]. The implementation of the 12-month study visit to those who were ineligible owing to breastfeeding intention, refusal, or dropout followed the standard protocol [1]. All children who completed the study were given a certificate of completion at 24 months.

### Lactation support and complementary feeding

The lactation counselors provided breastfeeding guidance to all mothers during the first 24 hours after birth and on days 3, 7, and 14, and were available for home consultations at other times. A telephone hotline was made available for emergency support seven days a week from 8 am to 5 pm. At three and six months, the mothers were contacted by telephone by one of the supervisors or lactation counselors. At three months exclusive breastfeeding was encouraged, and at six months the mother was encouraged to continue breastfeeding and given advice on complementary feeding. If a mother planned to start working outside the home and would not have the baby with her, a lactation counselor made an appointment to teach

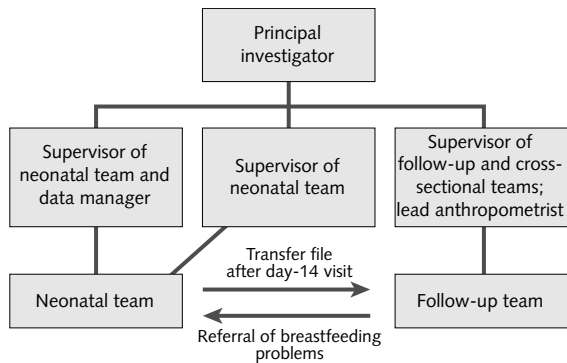


FIG. 2. Organizational and team coordination chart

her how to extract breastmilk (and, if necessary, left a breast pump with her). A counselor also contacted a mother when she experienced breastfeeding problems or the follow-up team was concerned that breastfeeding might be terminated before 12 months.

Complementary feeding guidelines were developed by the site's coordination team. Draft guidelines were sent to local pediatricians for comment and subsequently were revised based on their input (table 2). The guidelines were provided to all mothers. If a mother asked for advice on complementary feeding, the assistant referred to the guidelines but did not interfere with her physician's advice.

## Implementation of the cross-sectional study

### Sampling strategy

The limited population of Davis and the MGRS protocol requirement to minimize subject participation in both the longitudinal and cross-sectional components required local adaptations. The cross-sectional study adopted a mixed-longitudinal design, in which each child would be measured three different times at three-month intervals. Also, because of funding delays, the cross-sectional study at the United States site could not begin until after the longitudinal study subjects began to enter the age range of the cross-sectional study (18–71 months), and for this reason the target age range was restricted to 27 to 71 months. The mixed-longitudinal design and likely attrition rates set the target sample size at 483.

The sampling strategy was based on the index household method. Index households were defined as those that had been screened for the longitudinal study. Because nearly all births to Davis mothers in 1999 were screened for the longitudinal study, this approach did not bias the sample. The city was divided into 83 neighborhoods. The number of cross-sectional study subjects to be recruited from each neighborhood was based on its number of index households.

TABLE 2. Complementary feeding guidelines at the USA site

<p>Introduce solids, starting with small amounts, one or two times per day and gradually increase to three meals per day by 12 months, with additional snacks as desired</p> <p>The order of introduction of solids doesn't seem to matter, but start one new food at a time and allow four to seven days to watch for any reaction</p> <p>Baby cereals that are iron fortified are a good source of iron and therefore are often recommended as one of the first foods.</p> <p>After the transition period (when new foods are introduced), include fruits, vegetables, and high-protein foods (meat, fish, or eggs) every day. Include vitamin A-rich fruits and vegetables</p> <p>Do not feed more than 8 ounces of juice per day</p> <p>If there is a family history of allergies, don't feed eggs until the child is two years old, and don't feed peanuts, nuts, or fish until the child is three years old</p> <p>Continue to breastfeed as often as your baby wants. If you supplement, use cow's milk formula, NOT regular cow's, goat's, or soy milk before 12 months</p> <p>Start with pureed or strained foods, then mashed or finely chopped foods at 8 to 10 months, and most family food after 12 months (when more teeth are in)</p> <p>Fluoride drops are recommended where nonfluoridated water is used</p> <p>Iron drops are recommended for low-birthweight infants (beginning at 1 month, through 12 months)</p> <p>Vitamin D supplements are recommended for dark-skinned infants or those who get insufficient sunlight</p> <p>For those children who eat few or no animal products and show signs of poor appetite, a multivitamin (containing zinc) is recommended</p> <p>Make mealtime a happy, pleasant experience. Do not force your child to eat certain foods or finish everything on the plate</p>
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The recruiters identified each index household and went door-to-door in a clockwise direction to obtain information on the households closest to each index household. To determine the order of potential enrollment, the index households within each neighborhood were randomized. After the eligible children from the index households had been recruited, the children from nearby households were enrolled, starting with the household closest to the first index household, then the household closest to the second index household, and so on. The children in the set of next closest households were then enrolled. This continued, moving further and further from each index household, until the target number of subjects for each neighborhood was reached.

The selection criteria were consistent with the general MGRS protocol, except that children born outside of Davis were not excluded. Children enrolled in the longitudinal study were potentially eligible for the cross-sectional study, but a "cap" was placed on the percentage in the youngest age ranges that could participate in both components. The cap was based

on the estimated proportion of cross-sectional study children who, given the city's demographics, would have been in the longitudinal study. The maximum allowable percentage of longitudinal study children was 17% in the 27- to 30-month interval, 11% in the 30- to 33-month interval, and 6% in the 33- to 36-month interval. There were no longitudinal study subjects in the cross-sectional sample other than in those age groups.

If a household had more than one child who qualified, all were selected. The only exception was for siblings of subjects screened for the longitudinal study. We selected one such sibling for every third household screened for the longitudinal study that had more than one child who qualified (based on achieving a similar proportion in the cross-sectional study sample as these siblings would represent in the general population of Davis children 27–71 months of age).

### **Screening, enrollment, and survey logistics**

The cross-sectional study recruiters went door-to-door during the daytime and early evening hours seven days a week. Flyers with a postage-paid reply form were left at homes where no contact was made. If the form was not returned, up to two additional attempts were made (at least one of which was after 5 pm or on a weekend) to find someone at home. Neighbors were also asked about whether there were any children under six in the targeted households. If at least one neighbor was sure that no child in that age range was part of that household, the household was excluded.

In each neighborhood, the five households closest to each index household were contacted initially. On the first visit, the eligible children in the index household or the next closest household were enrolled, but children in all other households were put on a waiting list until complete information was available for all five households nearest to each index household. If at this point the target number for the neighborhood had not been reached, the process was repeated with the next closest set of five households.

## **Standardization, quality control, and data management activities**

### **Anthropometric standardization sessions**

Initial anthropometric training was conducted by the local lead anthropometrist, whose measurement techniques were standardized against the WHO lead anthropometrist before the initiation of the study [4]. The members of the neonatal and follow-up teams participated in standardization sessions with the cosupervisors and the local lead anthropometrist.

The neonatal team standardization sessions could

not be conducted in hospital newborn nurseries. Therefore, the mothers of young infants not enrolled in the longitudinal study were recruited to participate in specially conducted standardization sessions held at the site's coordination center. To ensure that the measurement techniques used with newborns did not differ from those used during standardization sessions, the lead anthropometrist observed at least one newborn measurement per week at the local hospital. During the first year of the study, neonatal team standardization sessions were held on a weekly basis for eight consecutive weeks to accumulate the data required for calculating reliability (precision and accuracy) statistics. Because the team was large, an algorithm was designed by the site statistician that permitted each infant to be measured by only four observers. This required 21 infants over a period of eight weeks, with each observer measuring 12 infants. This design allowed estimates of accuracy and precision similar to those required by the standard MGRS design [4].

The alternative algorithm described above was not required for the follow-up team. Standardization sessions were held at the coordination center or at local day-care centers. In general, five children aged 2 to 66 months were measured at each session. The data from two sessions were combined to obtain the required estimates of accuracy and precision. The accuracy and precision of each team member's measurements were reviewed after each standardization period, and corrective standardization sessions were scheduled for individuals whose measurement techniques needed improvement.

When the cross-sectional study began, the team participating in this component joined the remaining follow-up team members for anthropometric standardization sessions. Because the follow-up team helped out with the cross-sectional measurements, all personnel at that time were trained and standardized for measurement of height.

### **Motor development standardization sessions**

To ensure standardized data collection, the sites were required to conduct regular motor development standardization sessions [3]. However, by the time the standardization protocol was finalized, the US site had nearly completed collecting motor development data. Thus, only one standardization session was held following the standardized protocol. The initial training and standardization at this site were conducted at local day-care centers prior to the initiation of data collection with the assistance of a local expert (Dr. Ernesto Pollitt).

### **Quality control activities**

All quality control procedures in the MGRS protocol were followed [1]. During the first few weeks of the



study, the supervisors accompanied the fieldworkers on several home visits. Thereafter, random monitoring of data collection (10% of all interviews) was conducted by telephone. The supervisors served as backup data collectors and routinely observed the interviewing and measurement techniques of all study assistants.

The questionnaires were turned in to the supervisor daily and checked for completeness and consistency. Corrections were made when necessary. This sometimes required telephoning the mother or remeasuring a child. Any problems found during routine questionnaire checks were discussed at the next team meeting.

All team members attended regular staff meetings. In the longitudinal study, each team met with the supervisor weekly in the first few months and at least once every two weeks thereafter. These operational procedures provided abundant opportunities to oversee the quality of the work being performed.

### Data management

After reviewing all questionnaires, the supervisors coded the responses to any open-ended questions and forwarded the forms to data clerks. The data manager conducted data cleaning and validation (e.g., checking for outliers, data entry errors, and out-of-range values), completed preliminary data analyses, and prepared

the data files for transfer to the MGRS Coordinating Centre in Geneva.

### Conclusions

There were several challenges in implementing the MGRS protocol at this site, particularly during the neonatal phase. First, maintaining adequate daily communication with hospital staff was sometimes difficult. It required building good working relationships and perseverance. Mothers were sometimes not receptive to being screened so soon after delivery. This required making all mothers (and their physicians) aware of the study before hospitalization. Performing infant length measurements in the hospital was sometimes difficult when the infant became agitated. The mothers were reassured that the procedure was brief and not painful. In general, the mothers needed frequent breastfeeding support and assistance, and therefore additional lactation consultants were hired. During the follow-up phase, scheduling visits was a challenge that required persistence and flexibility. For example, if mothers were working outside the home, visits were scheduled at day-care centers. In terms of overall management, the greatest challenges were scheduling standardization sessions and mastering the data management system.

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